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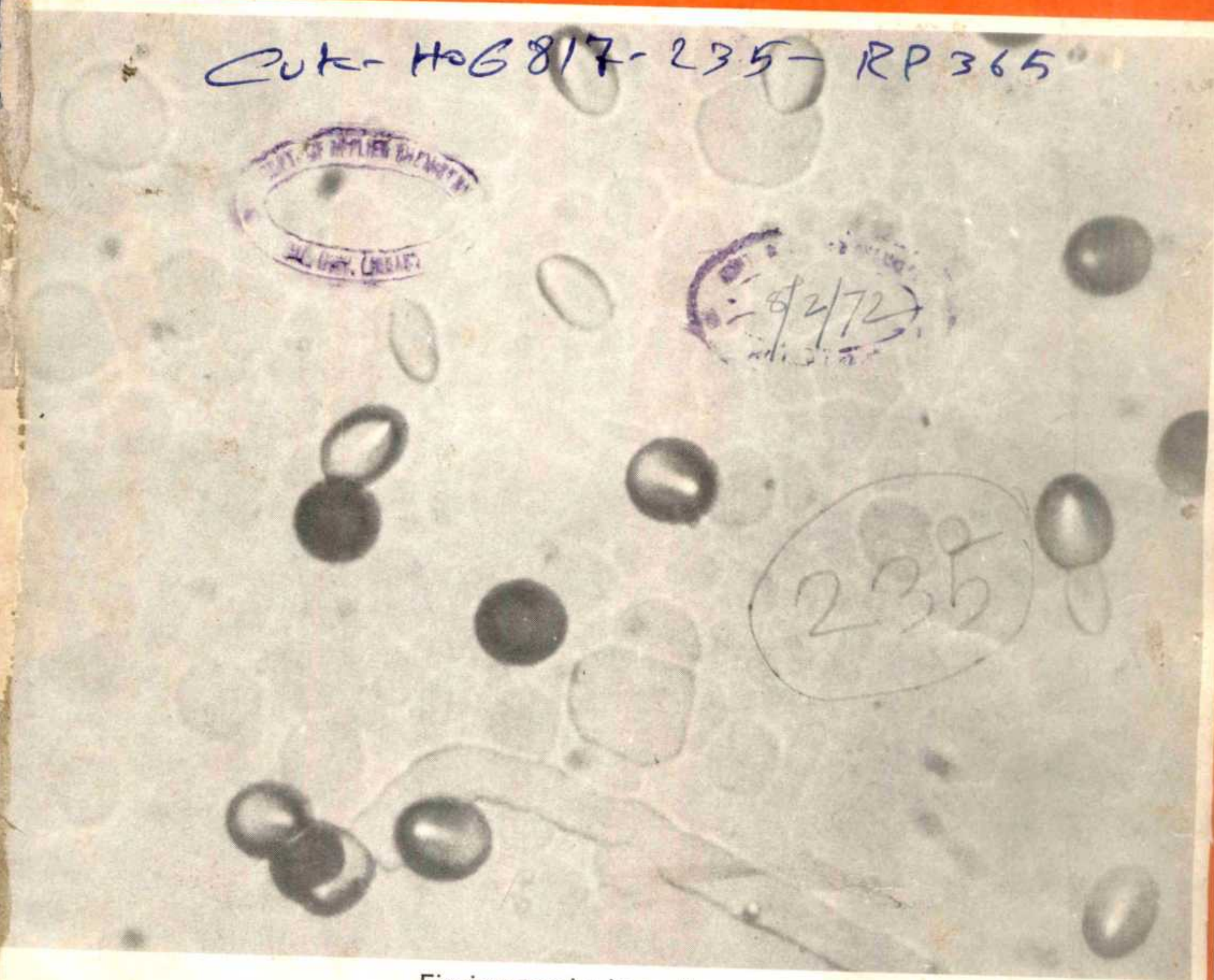

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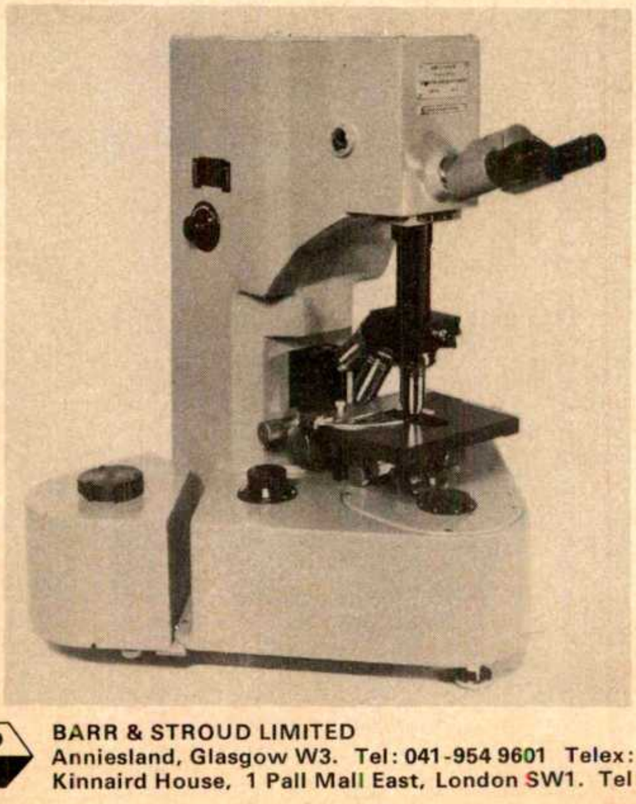

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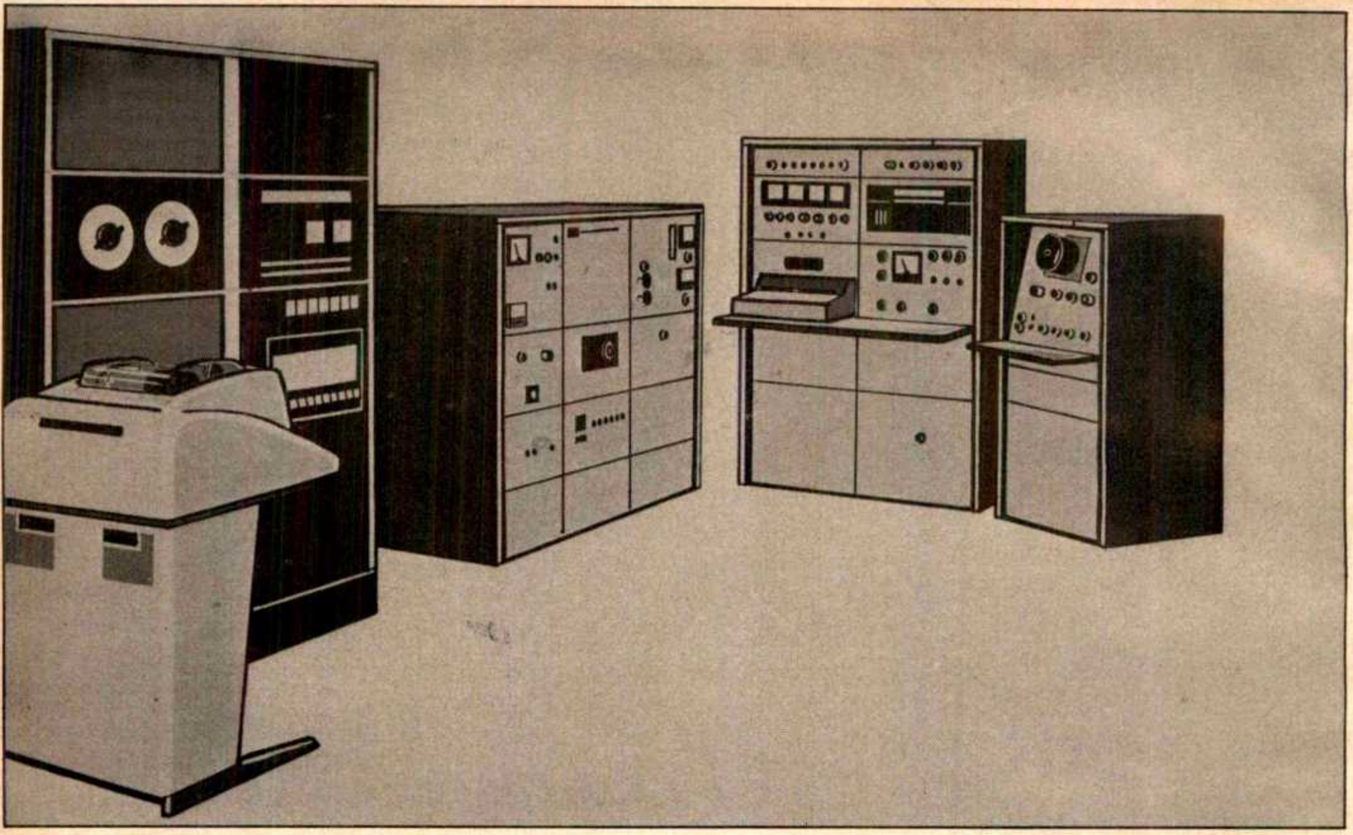

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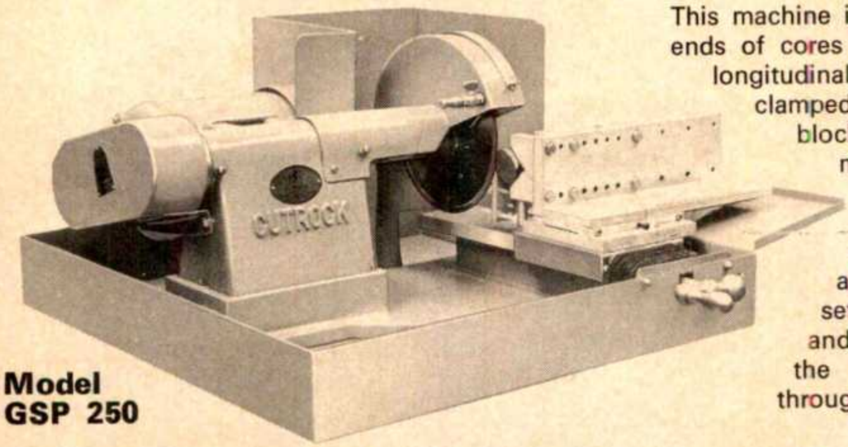

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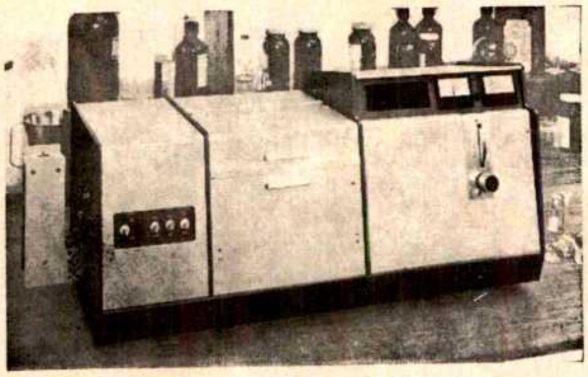

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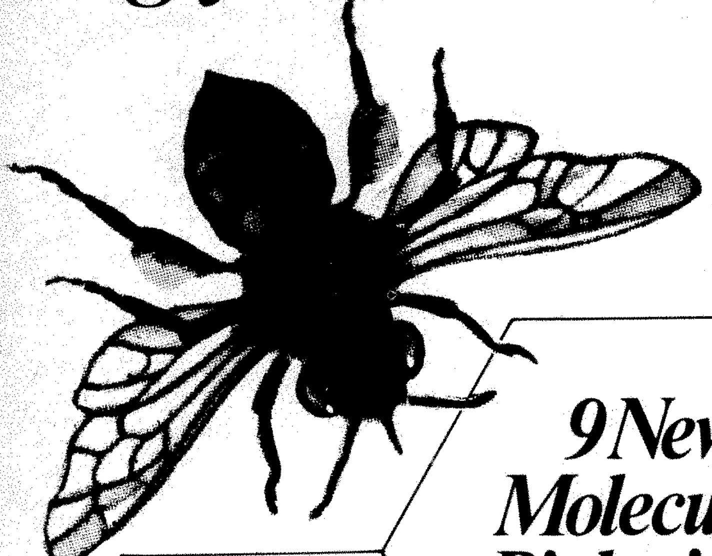

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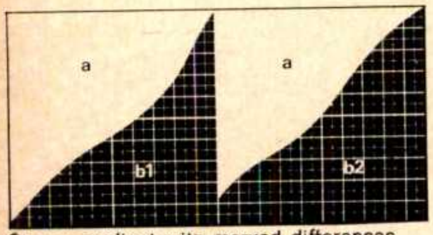

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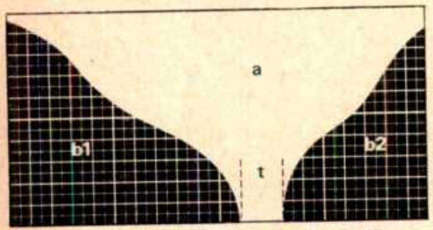

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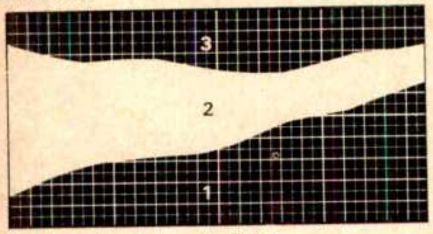

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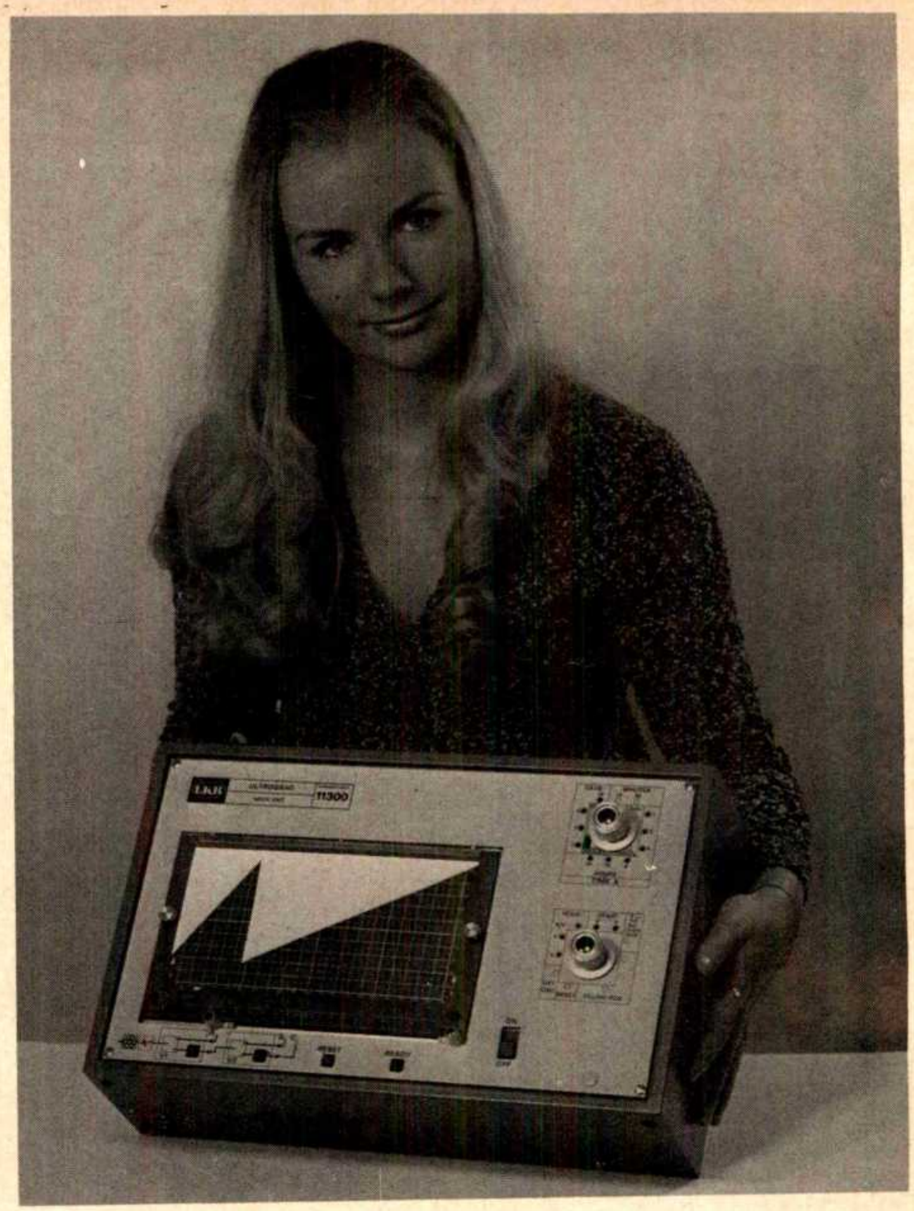

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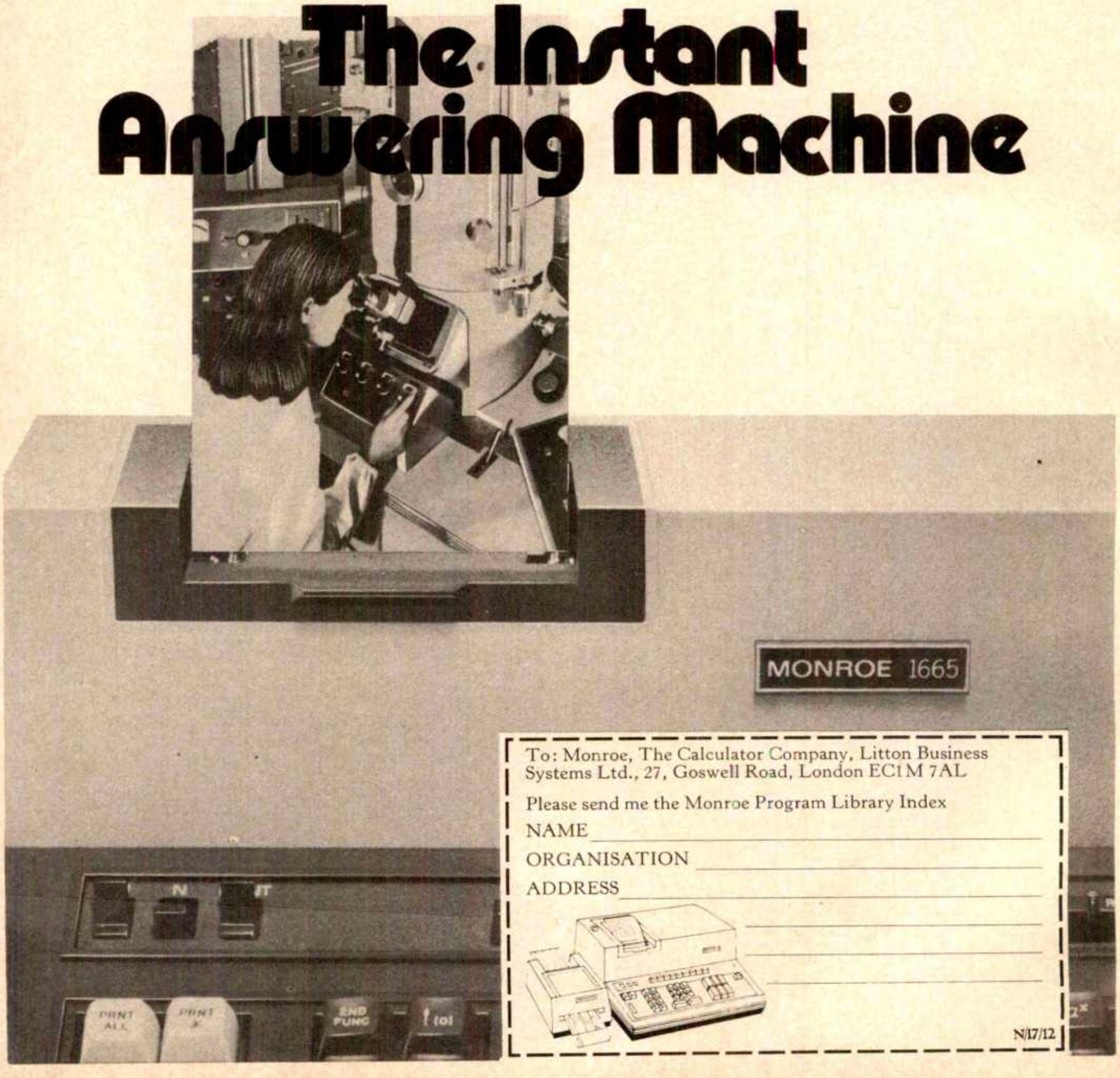

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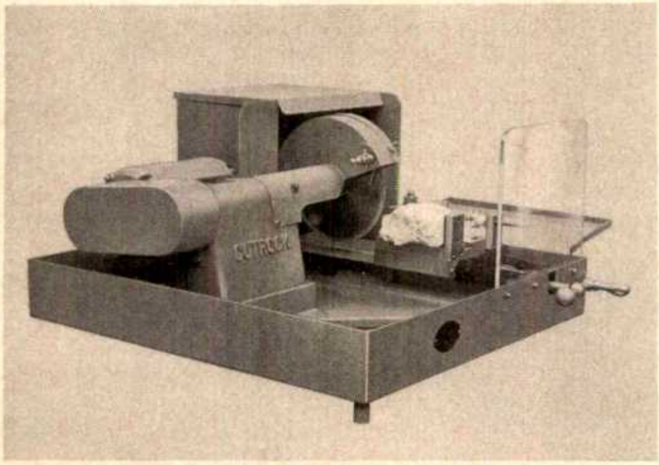

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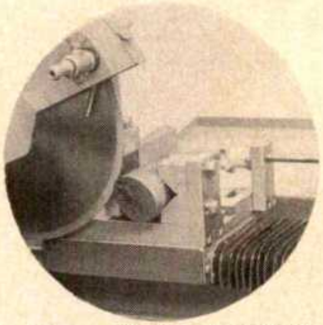

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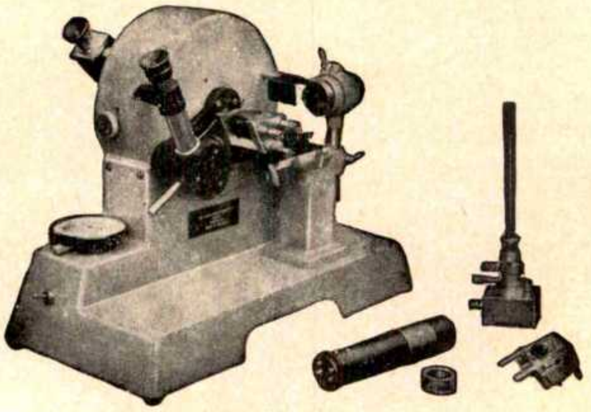

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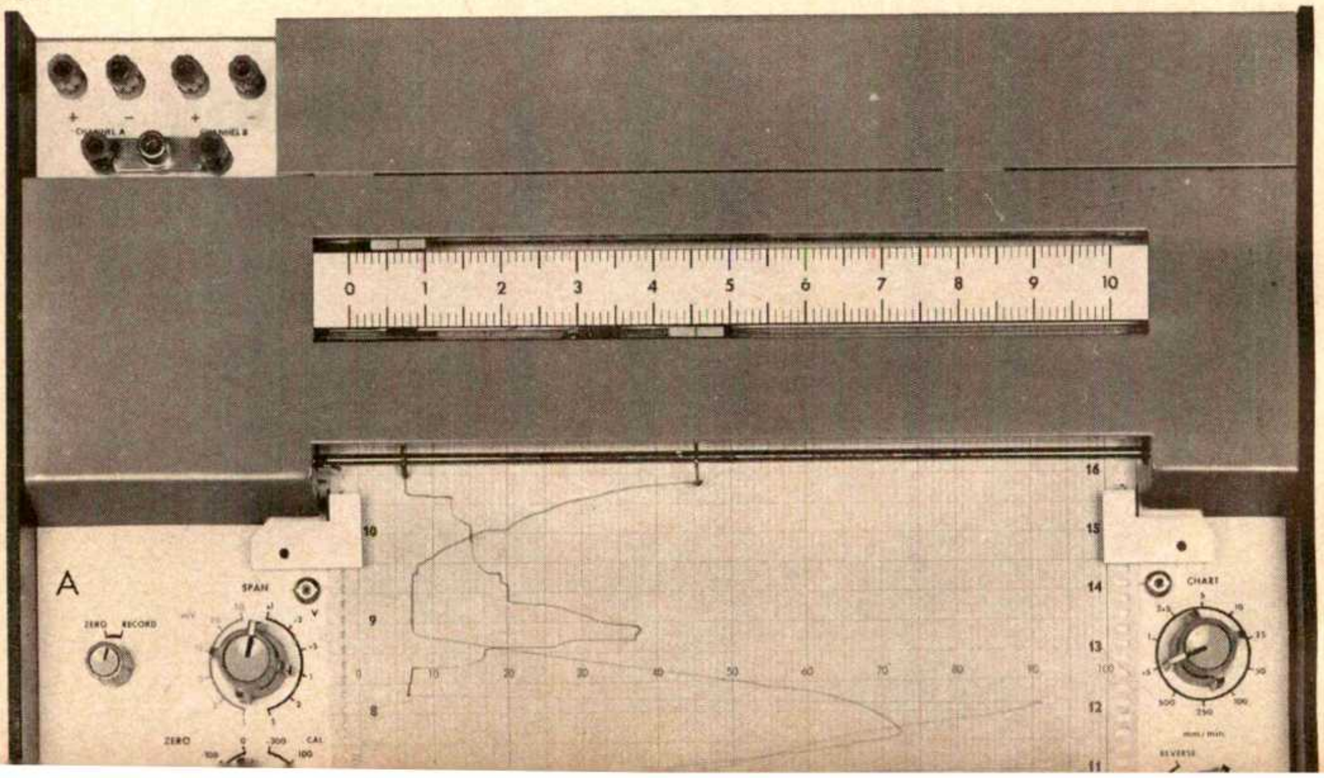

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Immunology—Selective stimulation of IgM synthesis in mouse B lymphocytes by pokeweed mitogen—PARKHOUSE, JANOSSY and GREAVES (MRC, Mill Hill)

Feedback Mechanisms in Animal Behaviour

D. J. McFarland

December 1971, xii+280 pp., £3.80

The work aims to introduce biologists who have a limited knowledge of mathematics to the principles of those aspects of control theory relevant to the study of animal behaviour. An attempt is made to facilitate an intuitive understanding of these principles without introducing high mathematical concepts such as complex numbers. Simultaneously, advanced aspects of control theory, such as optimization theory, which are highly relevant to the study of behaviour are discussed.

The Alpha Automatic Programming System

The Automatic Information Centre Studies in Data Processing No. 7

edited by A. P. Yershov

December 1971, xii+248 pp., £5.00

This collection describes the ALPHA system of automatic programming, based on 'Source language'—a somewhat modified version of the international programming language ALGOL 60. The fundamental part of the system is the ALPHA-translator—the compiler programme which carries out the conversion of programmes written in 'Source language' into working programmes in the language of M-20 machines: this is described fully.

Proceedings of a symposium on Comparative Genetics in Primates and Human Heredity held at Ernice, Sicily, in July, 1970

Comparative Genetics in Monkeys, Apes and Man

edited by A. B. Chiarelli

December 1971, x+346 pp., £5.50

Although scientists have readily adopted new techniques devised for the study of genetics, they have made little use of comparative research on the hereditary characteristics of the human species and other primates. It is certain that this offers a valid means of improving the progress in this area, which is of great importance to the future of Mankind. The aim of this book is to stimulate deeper research in human genetics and other fields concerning non-human primates.

The Biology of Lampreys Volume I

edited by M. W. Hardisty and I. C. Potter

December 1971, xiv+426 pp., £7.50

In recent years many significant advances have been made in the study of lampreys both during their larval life as microphagous feeders and as parasites in their adult stage. Unlike the hagfishes (the only other extant agnathan or jawless vertebrate group), no attempt has been made to collate and review these more recent developments. Students of vertebrate zoology will appreciate the detailed background information on the systematics, life histories, ecology and behaviour of lampreys, which for the first time has been collected in a complete treatise.

Advances in Drug Research Volume 6

edited by N. J. Harper and Alma B. Simmonds

December 1971, viii+256 pp., £5.00

A comprehensive and clear guide to the Hansch method of structure-activity correlation is provided by a medicinal chemist. Biochemists and pharmacologists at Duke University, USA, bring up to date molecular aspects of storage and uptake of noradrenaline and other catecholamines. Pharmacologists at the Max-Planck-Institut in Germany correlate the activities of morphine-like analgesics with their kinetics of distribution. A chemist at the School of Pharmacy, London, describes ways of using mass spectrometry in drug research, not only for structure elucidation but also its applications to analysis, metabolic and stability studies.

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NATURE Volume 234
NOVEMBER 5 1971

Will the Test Ban Ever Become True ?

THESE are confusing times for those who hope that the partial test-ban treaty will one of these days be extended to cover explosions beneath the ground. In the United States (see page 6) President Nixon seems finally to have agreed to let the underground test in the Aleutians take place. The Joint Committee on Atomic Energy in Washington has also been mulling over the question—the chances are that it will accept the Department of Defense's view that it would be unwise at this stage to extend the partial test-ban. Indeed, the seismologists are understandably divided on the issue—some of those who gave evidence in Washington last week were confident that it would be feasible promptly to extend the test-ban to cover underground tests, but others thought the time had not come. From a strictly technical point of view, this ambivalence is borne out by the 1971 progress report of the Stockholm International Peace Research Institute (SIPRI) on *Seismic Methods for Monitoring Underground Explosions*, Dr David Davies's latest supplement to the first report on seismic detection methods now distributed from Stockholm. The improvements of technique in the past two years have been considerable—new instruments now being laid out should make it possible two years from now to discriminate between explosions and earthquakes by remote methods where the explosions are equivalent to ten kilotons detonated in hard rock. There is even a chance that the limit of discrimination will settle at two kilotons when there is more experience of the advanced instruments.

The Cannikin test in the Aleutians is worrying for several reasons. It will most probably not trigger off an earthquake, and to that extent the Atomic Energy Commission was probably within its rights. The ecological dangers of which people have spoken are themselves ill-defined and improbable, although the way in which the Council on Environmental Quality has declined to comment on the AEC's environmental statement is a slap in the face for those who have been waiting for great things from the council. The real objection to the Cannikin test is political. For one thing, it gives offence to neighbouring countries, Canada and Japan in particular. For another, since it seems to be acknowledged that the test is part of the programme to develop warheads for anti-ballistic missiles, the occasion seems to serve notice that the SALT talks are making less rapid progress than people had been hoping. Dr James Schlesinger, the chairman of the AEC, said last week that he did not expect the tests to affect the talks ; most of his listeners will believe that that can be true only if the talks are going badly. It is true, of course, that the Soviet Union has only recently fired an underground explosion in its testing ground at Novaya Zemlya, so that both partners in the talks seem to be following the same despondent line. Unhappily, even here the facts are not clear. The AEC says that the most recent Russian test was of a weapon with a yield of three megatons or more, but the calibration of the magnitude of the surface waves produced by explosions of different power (reported by Dr P. D. Marshall and his colleagues on page 8) suggests that the Russian explosion most probably had a power less than 1.5 megatons. The amplitude of the surface waves have after all been published. The question in people's minds is bound to be whether the AEC is trying to make five megatons in the Aleutians seem a little more palatable to everybody by exaggerating the size of the explosion.

The difficulty of discriminating between underground tests and earthquakes will, in principle, never be solved. The more sensitive the instruments become, the greater will become the number of tiny earthquakes which they record and the greater will be the possibility that quite small nuclear explosions will go undetected. And it will not be long before instruments are refined to the point at which it will be necessary to distinguish nuclear explosions from other artefacts—ordinary chemical explosions, for example. In other words, there is plainly a limit to the perfectibility of a monitoring system operated by remote control. The practical question is, therefore, to decide at what point in the progressive improvement of seismic detectors it will be best to say that the time has come to settle for a treaty.

What are the risks ? The United States Congress and those government departments which fan its suspicions of any agreement that lacks provision for on-site inspection will always of course be able to shelter behind the view that no treaty can bring utter security. Any comprehensive test-ban treaty based on remote control is bound to allow some small explosions to go undetected. The question, from the point of view of the United States, is whether the Russian government has a military need to test weapons with an explosive power of a kiloton or two, whether it would risk the contumely of being discovered by some other method—espionage, perhaps—to have broken a treaty for the sake of such miniscule explosions and whether, in any case, there would be a military advantage in making such tests. After all, the days of the tactical nuclear weapon are over. In short, the point has probably been reached when a slavish insistence on on-site inspection has come to seem an attempt to avoid what could be an exceedingly valuable international agreement. The longer this goes on—and the Soviet government is as much to blame as the American—the more discreditable it will seem.

Alice Economics

Now that Mr Edward Heath has won his majority for the right to spend the coming year battling legislation concerned with the European Communities through the House of Commons, the recriminations are bound to be thrown thick and fast. The oddest so far is from Professor R. S. Scorer, professor of mathematics at Imperial College, London, who was complaining in *The Times* last week that the debate about British entry into the European Communities has ignored "the main issue of our time—how to control the pollution and the population explosion". He went on to say that the chief argument for membership is that it will "make the rich richer", but that "it is very dangerous to commit ourselves further to driving industry forward on those conventional lines which have brought about our predicament. . . . Member countries need to commit themselves as a matter of urgency to stopping the pollution which is rendering every sea around Europe useless in the biological cycle which is necessary for our continued existence. The rosy future in Europe seen by our leading industrialists is short-term only—it is physically impossible for it to endure."

The chief difficulty is, of course, to know whether Professor Scorer wishes to be taken seriously. What he seems to be saying is that even as things are, Europe is heading for a sticky end. If Britain joins the European Communities, as it will (Mr Harold Wilson notwithstanding), then the pace of economic growth will accelerate, the accumulation of pollution will accelerate, and the end will come sooner. This argument is false both in its premises and in its logic. Is it possible that Professor Scorer has been trying to provide the British public, and especially those parts of it which happen to read *The Times*, with a caricature of the arguments now constantly advanced by the environmentalists?

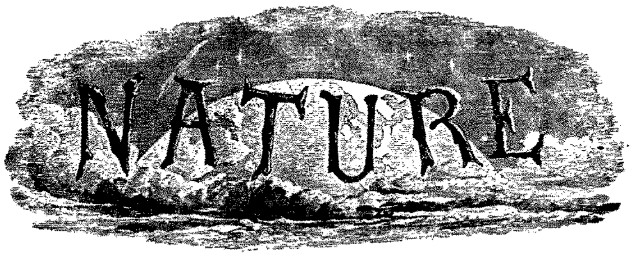
The premises are false in all kinds of amusing ways, but a list of them may help to warn off young people and other innocents. First of all, it is, as Professor Scorer no doubt wished to demonstrate, false to say that economic growth necessarily brings pollution. Indeed, in present circumstances, economic growth is probably a prerequisite for sensible measures for looking after the environment. Is it any accident that the richest nation in the world should now be the one making the most fuss about pollution ? Is there anything but economic growth that will allow the people of India to get rid of pollution of the environment by the cholera organism ? And if Europe wants to pay more regard to the condition of its environment, will it not be necessary to have at least enough economic growth to pay for all the extra sewage plants and government inspectors that that laudable task will require?

In Professor Scorer's little joke, the second false premise is that pollution is making the European seas "useless in the biological cycle which is necessary for our continued existence". Precisely what form of pollution he has in mind is hard to see. The beaches are more heavily polluted with flecks of oil than they have been for many years: nobody will deny that. But is there any evidence that British waters, say, have been rendered unproductive by pollution ? It is true, of course, that herrings are now much harder to come by in the North Sea, but the reason for that is over-fishing. There is a risk that other species of fish—haddock and cod, for example—will also be damaged in the same way. Salmon are also under pressure because of the new commercial fishery off the coast of Greenland. No doubt there is a great deal to be done to regulate these matters more sensibly, but law and regulations (or the lack of them) seem to be more important causes of potential trouble than pollution.

The belief that a larger European economic unit will "only help to make the rich richer" is of course an ambiguous remark—does Professor Scorer refer to people or to nations? If he has people in mind, there is a wealth of evidence to show that for a single economic unit, economic growth is one of the best ways to a greater measure of equality. If his remark had been intended seriously and had been directed to the gulf between the rich nations and the poor nations, it is hard to see how the emergence of an economically powerful European economic entity would be necessarily a bad thing. But surely what would matter is whether the European Communities would be liberal in their policies on foreign aid.

Professor Scorer's little joke would be harmless enough if it did not use some of the language which is by now widely used by those who seem to think that the world is about to end. That other mathematician, Charles Lutwidge Dodgson, sought to warn his young readers away from ill-defined heresies by means of allegory, but some people think he was too obscure. Professor Scorer's letter to *The Times* may have fallen flat for the same reason, for there will be many who will think he meant it to be taken seriously.

100 Years Ago



From an obituary of Charles Babbage by Professor W. S. Jevons.

> Of all Mr. Babbage's detached papers and volumes, it may be asserted that they will be found, when carefully studied, to be models of perfect logical thought and accurate expression. There is, probably, not a sentence ever penned by him in which lurked the least obscurity, confusion, or contradiction of thought. His language was clear, and lucid beyond comparison, and yet it was ever elegant, and rose at times into the most unaffected and true eloquence. We may entertain some fear that the style of scientific writing in the present day is becoming bald, careless, and even defective in philosophic accuracy. If so, the study of Mr. Babbage's writings would be the best antidote.
>
> Let it be granted that in his life there was much to cause disappointment, and that the results of his labours, however great, are below his powers. Can we withhold our tribute of admiration to one who throughout his long life inflexibly devoted his exertions to the most lofty subjects ? Some will cultivate science as an amusement, others as a source of pecuniary profit, or the means of gaining popularity. Mr. Babbage was one of those whose genius urged them against everything conducive to their immediate interests. He nobly upheld the character of a discoverer and inventor, despising any less reward than to carry out the highest conception which his mind brought forth.

From Nature, **5**, 29, *November* 9, 1871.

OLD WORLD

EUROPEAN LABORATORY

Italian Threat

THE Italian government has threatened to withdraw from ESRO unless its plans for the future of ESRIN, presented to the ESRO council at its meeting in Paris last week, are accepted. The future of ESRIN has been in the balance since it was announced last July that pure research had no part in the future of ESRO.

The hope that ESRIN can be maintained in its present form comes in a resolution submitted to the ESRO council by the Italian delegation at a meeting held on October 26. The closure of ESRIN would affect the Italians more than any other ESRO member and the threat made by Italy to withdraw from ESRO will possibly change the course of the council's action. The Italian delegation proposed that ". . . in a spirit of cooperation some of the ESRO buildings should be transferred to Italy and the remaining buildings should house ESRO work devoted to coordination and analysis of data relating to space missions in the scientific and applications field". The threat of withdrawal is made by the delegation when it continues, "It cannot, however, fail to point out that if it were impossible to reach agreement along these lines it would have serious effects on Italian participation in the organization's programmes."

The council has responded to the threat by inviting the Italian delegation to get together with the director general of ESRO, Dr Hocker, in order to set up a working party to investigate the possibility of such an arrangement. The working party is, however, working to a deadline as the proposals made in July are due to be ratified at an ESRO council meeting to be held in late November, and the council has allowed until November 15 for the working party to report on whether the proposed Italian solution is workable.

Scientists at ESRIN are unhappy about the possibility of the laboratory being split as the conditions of employment within ESRO differ considerably from conditions within Italian national laboratories It remains to be seen that if the Italian solution is the only one put forward whether it will be accepted by the ESRIN scientists.

An assurance was given at the council meeting last week that ESRIN would still be supported by ESRO until the end of 1973. An ESRO spokesman said this week that it was essential for work in progress to be completed and the present budget of \$2 million would be decreased to \$1.5 million in 1972 and \$1 million in 1973. This can be compared with the present ESRO scientific budget of \$27 million.

The staff of ESRIN is naturally embittered at the way the decision was taken to cease supporting the laboratory and this has in no way been helped by the attitude of the ESRO council that has forbidden the ESRIN director and staff members from communicating with the press. That this has irritated Dr N. D'Angelo, the present director, is shown in the following exchange of telegrams between ESRO headquarters at Paris and ESRIN. The following is the text of a message from ESRO in Paris to D'Angelo with a reply sent the following day, October 15.

"In present circumstances the directorate believes that it is preferable not (repeat not) to accord interviews. As you know the situation is still fluid and decisions on ESRIN and other parts of ESRO remain to be taken at the end of November. A full statement will be made at that time and in the meantime director general's policy is not to seek publicity or to reply to provocative articles beyond correcting gross factual errors."

The reply from D'Angelo was: "Ref. your memorandum concerning statements attributed to me. . . . Do not understand how it can be not opportune to correct gross factual errors made in attributing to me some statements which I had not made. Not in real interest of organization, quite apart from fact that my own name has been misused."

There is no doubt that ESRO headquarters in Paris are being unrealistic in hoping that the staff of ESRIN will accept their fate quietly. The scientist will not rest quietly while the door of opportunity is being slammed in his face.

NOBEL PRIZE

Father of Holography

THE 1971 Nobel Prize for physics has been awarded to Professor Dennis Gabor, of Imperial College, London. It comes as something of a surprise that the award is made for Professor Gabor's "invention and development of the holographic method" alone rather than in recognition of his broader contribution to physics. For although Professor Gabor is recognized as the inventor of holography, the technique lay dormant for more than a decade after the invention, first reported in *Nature* (**161**, 777 ; 1948). Since then, he has made significant contributions to fields as diverse as electron microscopy and cybernetics.

Born in Budapest in 1900, Gabor studied and worked in Germany until 1933, when he moved to England. The principle of holography which he developed is simple enough—an object is illuminated by a coherent electron or light wave, and the interference pattern resulting from the interaction of the secondary wave arising from the object with the strong background wave is recorded on a photographic plate. When the plate is illuminated by the strong background wave alone, the information which it contains about the object originally viewed can be extracted to give an image. As is often the case, however, it was a major step to develop practical holography from the first successful laboratory experiments.

Originally, Gabor hoped that holography would offer a new microscopic technique, because micrographs constructed using electron waves but "played back" with an optical synthesizer, should produce an image scaled up in the ratio of light waves to electron waves—some 100,000 times magnification. But this hope was unfulfilled, and the "electron interference microscope" did not then become a practical reality.

The chief difficulty with the Gabor method was the difficulty of separating the information required from a "conjugate wave" which may be regarded as attributable to a fictitious object similar in nature to the true object but occupying a different plane. With the advent of lasers, interest in holography revived because of the availability of coherent sources of optical light. But the technique remained practically unused until E. N. Leith and J. Upatnieks developed an improved wavefront reconstruction technique in the early 1960s. Leith and Upatnieks were also at the forefront of the development of three-dimensional holography.

In spite of practical difficulties, however, the basic principles of Gabor's method remain sound, and in this sense he is truly the father of holography. Indeed, the principle of the electron interference microscope has itself been vindicated. Holographic techniques have now been used by Professor George Stroke and his colleagues to improve the resolution of electron micrographs to 2.5 Å, revealing the internal structure of a virus (*New Scientist*, **51**, 671 ; 1971).

Extract from D. Gabor's original letter describing the technique now known as holography:

". . . the arrangement is similar to an electron shadow microscope; but it is used in a range in which the shadow microscope is useless, as it produces images very dissimilar to the original. The object is preferably smaller than the area which is illuminated in the object plane, and it must be mounted on a support which transmits an appreciable part of the primary wave. The photographic record is produced by the interference of the primary wave with the coherent part of the secondary wave emitted by the object. It can be shown that, at least in the outer parts of the diagram, interference maxima will arise very nearly where the phases of the primary and of the secondary wave have coincided.

"If this photograph is developed by reversal, or printed, the loci of maximum transmission will indicate the regions in which the primary wave had the same phase as the modified wave, and the variations of the transmission in these loci will be approximately proportional to the intensity of the modified wave. Thus, if one illuminates the photographic record with an optical imitation of the electronic wave, only that part of the primary wave will be strongly transmitted which imitates the modified wave both in phases and in amplitudes. It can be shown that the 'masking' of the regions outside the loci of maximum transmission has only a small distorting effect. One must expect that looking through such a properly processed diagram one will see behind it the original object, as if it were in place.

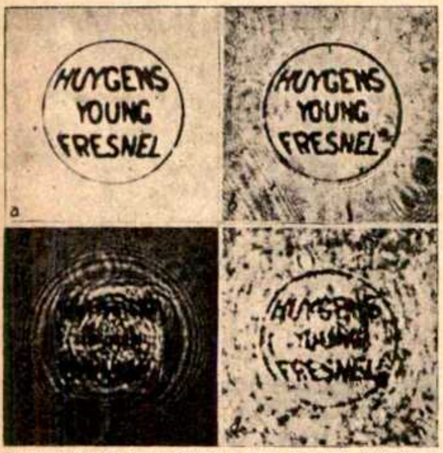


FIG. 2. (*a*) ORIGINAL MICROGRAPH, 1·4 MM. DIAMETER. (*b*) MICROGRAPH, DIRECTLY PHOTOGRAPHED THROUGH THE SAME OPTICAL SYSTEM WHICH IS USED FOR THE RECONSTRUCTION (*d*). AP. 0·04. (*c*) INTERFERENCE DIAGRAM, OBTAINED BY PROJECTING THE MICROGRAPH ON A PHOTOGRAPHIC PLATE WITH A BEAM DIVERGING FROM A POINT FOCUS. THE LETTERS HAVE BECOME ILLEGIBLE BY DIFFRACTION. (*d*) RECONSTRUCTION OF THE ORIGINAL BY OPTICAL SYNTHESIS FROM THE DIAGRAM AT THE LEFT. TO BE COMPARED WITH (*b*). THE LETTERS HAVE AGAIN BECOME LEGIBLE

"The principle was tested in an optical model, in which the interference diagram was produced by monochromatic light instead of by electrons. The print was replaced in the apparatus, backed by a viewing lens which admitted about sin $\alpha = 0.04$, and the image formed was observed and ultimately photographed through a microscope. It can be seen in Fig. 2 that the reconstruction, though imperfect, achieves the separation of some letters which could just be separated in direct observation of the object through the same optical system. The resolution is markedly imperfect only in the centre, where the circular frame creates a disturbance. Other imperfections of the reconstruction are chiefly due to defects in the microscope objectives used for the production of the point focus, and for observation.

"It is a striking property of these diagrams that they constitute records of three-dimensional as well as of plane objects."

(From *Nature*, **161**, 777; 1948.)

NOBEL PRIZE

Herzberg Honoured

THE 1971 Nobel prize in chemistry has been awarded to Dr Gerhard Herzberg for his work on the electronic structures and geometries of molecules, especially free radicals. Dr Herzberg created the sound basis on which modern molecular spectroscopy is built and it was his own dynamic and enthusiastic approach to the subject which made his laboratory at the National Research Council in Ottawa a mecca for spectroscopists and his books on spectroscopy standard works of reference.

Dr Herzberg was born in Hamburg in 1904 and took a doctorate in physics at the University of Darmstadt in 1928. After two years at the University of Bristol, he returned to Darmstadt where he stayed until 1935. He then spent ten years at the University of Saskatchewan before moving to Yerkes Observatory, Chicago, in 1945. It was there that he applied his spectroscopic expertise to studies of the molecular spectra of planetary atmospheres and, with near infrared absorption techniques, he reproduced many of these spectra in the laboratory using long tubes of gas at high pressures. The period at Yerkes also saw the birth of a fruitful working relationship with Edward Teller which led to the enunciation of the Herzberg–Teller spectroscopic rules.

Although Dr Herzberg is essentially an experimentalist, he has a thorough understanding of the theoretical principles of his work which contributes to the high quality of his three books on molecular spectroscopy. His investigations of the structures of free radicals made extensive use of the technique of flash photolysis and his interest in astrophysics was further stimulated by his study of radicals such as $-CH$ in the tails of comets.

Dr Herzberg's own achievements are many but his infectious enthusiasm and example must have inspired much more work than he himself has performed.

SPACE

Goodbye to All That

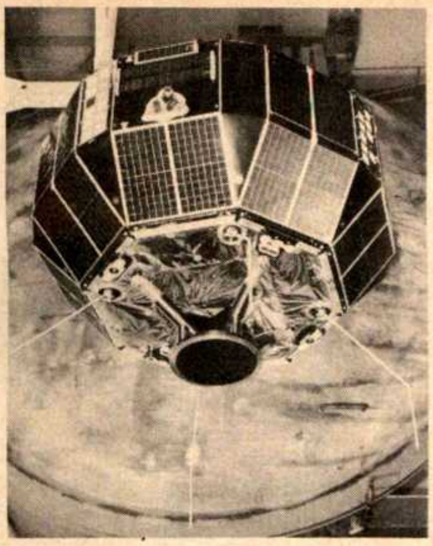
THE successful launch of the technology satellite Prospero on October 28 will in no way affect the decision to abandon Black Arrow announced in July (see *Nature*, **232**, 363; 1971). The satellite was launched at 0509 BST from Woomera and went into a near-polar elliptical orbit of 350 by 850 miles. The Black Arrow launcher worked perfectly after the one failure, one success and one partial success that make up its past history, and the experiments on board are all behaving normally. The useful life of the satellite will be between six months and a year, during which equipment for future space vehicles will be tested and a scientific experiment to measure the incidence of micrometeoroids—designed at the University of Birmingham—will be conducted.

Prospero—otherwise known as X3—is the second entirely British satellite to go into orbit, the first being the scientific satellite Ariel 3 in May 1967, but Prospero is the first to go up on a British launcher. The only other satellite at present planned under the national space technology programme is X4 which is due to be launched in 1974 on an American Scout rocket from the United States Western Test Range. Otherwise Britain's national space programme hangs fire until the government's review of it is completed early next year, although the scientific space research programme continues with the launch of UK-4 (Ariel 4), expected at the end of this month.

The decision to abandon Black Arrow was not taken because of the failure of the early launches so much as because the launcher was too small to put more than a low orbiting satellite into space and because of the high cost of the infrequent launches of the rocket. The average cost per launch of Black Arrow has been about £2 million whereas NASA will launch X4 for Britain for £1.25 million. Where the future of Britain's satellite programme may well lie—if it is to have a future—is in the larger geostationary satellites which cannot easily be launched from Woomera but which can be put into space from the USA. Hawker Siddeley, BAC and Marconi are at present studying designs of geostationary technology satellites (GTS).

Meanwhile Britain's active rocket engine industry is confined to supplying Skylark to ESRO and supplying Blue Streak to ELDO on a commercial basis —Britain having effectively withdrawn from ELDO by refusing to support an extension of it in 1968 and limiting commitment to £11 million from January 1, 1969. Further, it is most unlikely that Britain will attempt to develop a new launcher alone but will instead concentrate the limited money available—about £4.6 million a year at present—into British satellites launched from the United States. There is as yet no firm agreement with NASA that American rockets will be available to launch British satellites after X4 but suggestions that such an agreement may not materialize meet with bland assurances that there will be no problem.

Apart from Britain's own satellite work there is the possibility of British involvement in the post-Apollo programme, and both Hawker Siddeley and BAC are studying precisely what con-



Prospero, Britain's first technology satellite, now passing over the whole of the Earth's surface twice every 24 hours.

tribution they could make. Talks between NASA and the European nations, however, have so far produced no firm plans, and British withdrawal from the talks because the areas of co-operation were not sufficiently defined and because of the assumption behind the talks of a link-up between the post-Apollo programme and ELDO's Europa 3, in which Britain has declined to participate, will not have helped speed results.

HISTORY OF SCIENCE

Rutherford Remembered

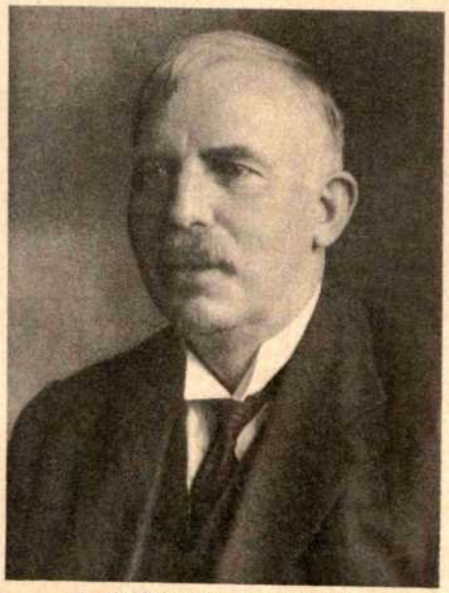
THE life and work of Ernest Rutherford were recalled last week during the British celebrations to mark the centenary of his birth in New Zealand. A visit to the Cavendish Laboratory and lectures in Cambridge were included in the programme, as well as three lectures at the Royal Society and a Friday Evening Discourse at the Royal Institution that was principally devoted to some of the elegant experiments which Rutherford himself performed.

Sir Mark Oliphant, one of Rutherford's co-workers at the Cavendish Laboratory, spoke at the Royal Society about Ernest Rutherford the man. But before delivering his own address, Sir Mark read some of the notes prepared by Sir James Chadwick who was to have lectured but was prevented from so doing by ill-health. Sir James had been planning to describe his first contacts with Rutherford while attending his undergraduate course on electricity and magnetism at the University of Manchester in 1909. During this time, Sir James recalls that he began "to realize what physics was all about".

Sir Mark Oliphant's own recollections of Rutherford were of a man who "looked more like a businessman or a Dominion farmer" and who seemed incapable of speaking in anything but loud tones "tinged with an Antipodean flavour". Many of Rutherford's habits were evidently trying for those who worked with him; he apparently possessed no fountain pen and would often perform rapid arithmetical calculations in an illegible fashion or attempt to mark film taken during an experimental run before it was properly fixed or dried. It seems that even Rutherford was criticized in the 1930s by the council of the then Department of Scientific and Industrial Research for not adapting his research to the needs of industry and for producing the wrong type of research worker; the concern about such matters shown by the research councils nowadays is evidently nothing new.

In the afternoon, Sir Harrie Massey sketched the developments during the twentieth century that had been a natural consequence of Rutherford's own work—including the identification of many elementary particles in cosmic radiation and of an even larger number at particle accelerators. Professor N. Feather said of Rutherford, Newton and Faraday that "each was in his own way unique, each in some ways unsurpassed, each a giant in our society's history".

In the best traditions, Dr T. E. Allibone, who also worked under Rutherford at the Cavendish Laboratory, lectured with a liberal sprinkling of experiments based on those performed by Rutherford himself. These included a demonstration of the magnetic deflexion of α-particles, using apparatus that was characteristically Rutherfordian in its compactness. The famous α-particle scattering experiment was shown off to particular advantage with the help of an image-intensifier which allowed the scintillations to be displayed on a closed-circuit television screen.



Lord Rutherford 1871–1957.

RESEARCH COUNCILS

Riding the Storm

THE Social Science Research Council was particularly concerned with finance during the past year and its plans for increasing support for research and training students received a severe setback when government support for the research councils was cut in the autumn of 1970. Mr Andrew Shonfield, then chairman of the council, says in the annual report that the cuts affected the SSRC more than the other research councils because a greater proportion of the SSRC's money is spent on student support, whereas the other councils could cut long-term projects without affecting postgraduate awards. (*Report of the Social Science Research Council April 1970–March 1971*, HMSO, £1.50.)

The theme of the report is the effect on social science research of the reduced rate of expansion imposed by the government. After the curbs placed on spending in 1970, the council had to restrict the number of studentships awarded in September 1971 to the number allocated a year previously. This reversal of the trend that had seen the number of new studentships increase from 903 in 1968–69 to 1,521 in 1970–71 was implemented by the council in the novel way of requiring third-year research students, who in previous years had their grants renewed automatically if their supervisors' reports were satisfactory, to compete with new research students for the limited number of awards. This approach, predictably, had its opponents in university departments who felt that a person of proven research ability should not have to compete with aspiring research workers, but the council felt that in this way it was being fair to the new graduates and such an approach ensures, of course, that the holders of awards apply themselves during the second year of their research work.

One of the pleasing aspects of the report is that the SSRC has been increasingly absorbed into the scientific community of the other four research councils and the Council for Scientific Policy. The council welcomes the challenge of having to compete with the other research councils for resources and Mr Shonfield looks forward to the day when the SSRC will be an organization that is comparable to the other research councils.

Nearly £2 million was committed by the council during 1970–71 for research in eleven major disciplines. These range from £390,942 allocated to management and industrial relations, to £30,362 allocated to human geography.

NEW WORLD

The Limits of Seismology

by our Washington Correspondent

THE Partial Test Ban Treaty was always supposed to be a temporary expedient —the best that could be achieved at the time. The treaty is now more than eight years old, and attempts to reach agreement on a more comprehensive arrangement have always fallen at the first hurdle—insistence by the US government on on-site inspection and the unwillingness of the Soviet government to consider such a proposal. In the meantime, nuclear weapons testing has continued—the chairman of the Atomic Energy Commission, Dr James R. Schlesinger, was telling the world only last week that President Nixon has now given the green light for the 5 megaton Cannikin test in the next few weeks.

To understand better the basis for the Administration's policies towards a comprehensive test ban, the Joint Committee on Atomic Energy last week held two days of hearings designed to assess the ability of seismologists to recognize signals from underground explosions. Four chief conclusions emerged from the hearings. First, the financial shot in the arm that the Defense Department has given to seismology since the partial test ban has produced some spectacular advances in monitoring techniques, but opinions differ on what can be accomplished. Second, the Administration is not yet prepared to change its views about on-site inspection, and the Joint Committee on Atomic Energy is unlikely to demand such a change of policy. Third, the funding of seismological research by the Defense Department is beginning to peter out. Finally, and perhaps most important, it is becoming increasingly clear that the chief decisions are now political and not technical.

In the past year there have been many claims and counter claims about the ability of seismologists to police a ban on underground testing, and the Defense Department's insistence on on-site inspection has been under increasing fire from some scientists and from the press. Some argue that present techniques and instruments suitably deployed could pick up all but the smallest explosions (down to one or two kilotons) while others maintain that a determined violator of a comprehensive test ban could use a variety of tricks to hide the seismic signals from even quite large underground explosions.

What is the ability of seismological techniques to discriminate between the signals of small explosions and of earthquakes? Both produce a variety of seismic waves that travel through the Earth and along its surface, but fortunately the signals from the two sources differ in such a way that it is usually possible to tell them apart. The most promising technique so far seems to be to measure the proportion of energy generated in the form of short period body waves (m_b) and long period surface waves (M_s). In general, earthquakes are more efficient generators of surface waves than are explosions.

There is a limit to which any technique is capable of picking up signals from either earthquakes or explosions, and that is regulated by the ever present background "noise"—signals from a variety of sources such as ground slippage, wind or traffic near the seismometers. This noise produces a constant interference signal which effectively masks the seismic traces from explosions or earthquakes equivalent to about one-half kiloton set off in hard rock. This has two important consequences—any test ban treaty would have to be undertaken with the knowledge that a violator could explode a very small weapon without fear of detection and that he may also be able to mask the seismic effects of larger devices so that they too would be lost in the background noise.

Another consequence of this theoretical detection threshold is that the body waves from a small underground explosion might be picked up by seismometers while the surface waves would be lost in the noise. In other words, a positive identification of an explosion as opposed to an earthquake may have to rely on the fact that surface wave signals are not detected. Asked last week whether he thought such a no-detection criterion to be a reliable basis for a comprehensive test ban, Dr Stephen J. Lukasik, director of the Defense Department's Advanced Research Projects Agency (ARPA), which has been responsible for the seismic detection programme, said that he believes not. The Defense Department's line therefore seems to be that positive identification of an explosion should rely on traces of both the body and surface waves—a criterion that raises the identification threshold considerably, and inhibits the likelihood of negotiating a treaty.

That apart, just how capable are present techniques of detecting explosions? That, at least, was what the Joint Committee on Atomic Energy was concerned to find out. Lukasik did not commit himself to any figure for the capability of the present system, but said "we understand how to identify explosions down to m_b 4.5" (equivalent to about five kilotons fired in solid rock) and that "in principle, seismic discrimination around m_b 4.0 appears feasible". This would take the level of explosion that could be detected by improving the seismic arrays down to about one or two kilotons in solid rock. But Dr Lukasik was quick to point out that not all the theoretical problems are yet solved. Explosions at that level would also be detected by the absence of visible surface waves. Dr Eugene Herrin later told the committee that we cannot at present "design an optimum seismic network nor can we reliably estimate the unilateral identification capability of a given network for events of magnitude less than about 4.75".

On the other hand, some seismologists argued at the hearings that a seismic array system can now be designed to monitor explosions down to one or two kilotons, and that such an array would be an adequate basis for policing a treaty banning underground testing. This argument has, in fact, caused considerable embarrassment to the Defense Department since it has been well aired in the press, and it has been billed as the conclusion of a meeting sponsored last year by ARPA. Moreover, in July this year, the Canadian delegation to the Committee on Disarmament seemed to be saying much the same thing.

One particular point that worries the Joint Committee on Atomic Energy is the extent to which a signatory of a comprehensive treaty could cheat with impunity. Witnesses last week faced a number of questions designed to ascertain the level to which this could be done. The committee was told that there are four potential methods by which a violator could hide signals from relatively large explosions in the background seismic noise. The signals could be damped by firing explosives in alluvium instead of solid rock or, by firing a device in a large cavity (uncoupling), it may be possible to fire off several devices in succession and so generate waves that look like an earthquake, or alternatively, a large device could be set off in the wake of an earthquake, and the seismic waves would be hidden.

Of these methods, only firing in alluvium has been extensively tested, and it is generally agreed that a 15 kiloton shot in alluvium would give about the same seismic signals as a one or two kiloton shot in hard rock. Uncoupling has only been tested once with a 0.3 kiloton explosion, but in theory it may be possible to hide an explosion of up to 100 kilotons by this method. Ripple firing has never been tested, and there are considerable doubts about its potential. Finally, hiding in an earthquake would not be a very practical alternative since it would entail sitting around with a device waiting to be set off until a suitable earthquake comes along.

Perhaps the most important unanswered question that came up in the hearings last week, and one which was not well dealt with, was what happens now with the ARPA seismic detection programme? Started in 1959, Project VELA, as it is known, has been responsible for the infusion of some $160 million into seismology.

There are essentially three options now open—to do nothing further on seismic detection and identification, but to concentrate on analysing the data from the three large arrays recently deployed in the United States and Norway (the LASA short period array in Montana, the ARPA long period array in Alaska and the NORSAR short period array in Norway), to upgrade the present system, or to push ahead with deployment of a full-scale monitoring system. Which option the government will take is now a political rather than a technical decision.

All three alternatives were mapped out by witnesses last week. A surveillance system based on the present reporting network would consist of selected stations of the Worldwide Standard Seismograph Network together with the three large ARPA arrays. At a very small cost, this system could be upgraded by the inclusion of five British array stations in Australia, Canada, Scotland, India and Brazil.

The most grandiose proposal was put to the committee by Dr James Brune, professor of geophysics at the University of California, San Diego. Brune's proposal, which apart from increasing the potential to detect small yield explosions would be a bonanza for geophysics, was endorsed by a list of names that looks like a *Who's Who* of geophysics. The proposal, which could be implemented in two stages costing $27.5 million and $106 million respectively, consists of large and medium aperture arrays in Europe and Asia, long and short period seismographic stations in Europe and North America, ocean bottom seismographs, and upgraded Worldwide Standard Seismograph Network stations. Such a system, Brune claims, would be able to detect and identify explosions equivalent to 2 kilotons in hard rock, without a serious false alarm problem from small earthquakes being misidentified as explosions. To judge by the questions from the members of the committee, it seems that they have no intention of rushing to buy the proposal.

Whatever array systems are deployed, the possibility of a violation of a comprehensive test ban treaty being undetected can never be reduced to zero. That is the chief reason why the US government has always insisted on the necessity for on-site inspection, and that is one reason why the Joint Committee on Atomic Energy has tackled a difficult problem. Some witnesses suggested last week, however, that on-site inspection may be a red herring, for not only would very small explosions go completely undetected, thereby providing no grounds for inspection in any case, but, as Lukasik himself admitted, on-site inspection would not necessarily provide evidence of a test.

The decision is now clearly a political one, and it must rely in part on the strategic advantage likely to accrue from testing the very low yield weapons that would not be picked up by seismographs. In his opening remarks last week, Melvin Price, the committee chairman, said that such issues may be explored in later hearings. It now seems that such hearings are vital.

NAS

Thorns in the Academy's Flesh

by our Washington Correspondent

Richard C. Lewontin, who resigned from the National Academy of Sciences in April in protest against the academy's acceptance of work on projects classified as secret, has been given a full year in which to change his mind. At a business meeting last week, attended by between 70 and 80 of the academy's 900 members, it was decided to postpone action on Lewontin's resignation until the annual meeting next spring. Technically, therefore, Lewontin remains a member of the academy—a situation which he described in his letter of resignation as repugnant.

Why has the academy not decided to let him leave without demur? The chief reason for postponing action on his resignation last week was that the academy has in the past few months moved some way towards meeting the objections raised in Lewontin's letter of resignation. Essentially, Lewontin was concerned that members of the academy are ultimately responsible for all work carried out in the academy's name, and that the acceptance of classified work therefore puts the members in the position of being responsible for reports that they are prevented even from seeing. A provision adopted at the August council meeting now requires that all academy reports should include a statement to the effect that only the members of the committee producing the report are responsible for its contents.

The academy has decided to see whether such a provision is a sufficient concession to enable Lewontin to remain a member. Lewontin's stand on classified research was endorsed by a few younger members of the academy, three of whom—Thomas Eisner and Bruce Wallace of Cornell University and Robert MacArthur of Princeton—said they would resign if the issues raised by Lewontin were not soon resolved. Asked last week whether the academy's concessions were enough, Eisner said that he at least would probably be satisfied, but added that he did not know the full terms of the provision.

Lewontin has also been critical of the academy's machinery for electing its officers, and this too has been liberalized, but according to Allen V. Astin, the academy's internal secretary, not simply in response to Lewontin's attacks. The chief change agreed at the meeting last week was that officers will in future be elected by a ballot among all members, not just those present at the annual meetings. It is also agreed that nominations can come from the floor of the annual meeting. In the past, a special nominating committee, appointed by the president with the advice of the council, has produced a slate of nominations that were then voted on by the members present at the annual meeting. (On at least one occasion in the past, however, the election of Dr Detler W. Brook as president in 1950, an unofficial nomination from the floor has carried the day.) In future, the nominations committee's list of candidates can be augmented by suggestions from the floor that are backed by at least seven members.

Another issue raised at the meeting last week has now become a regular feature of academy meetings. The membership voted down without debate a motion by William Shockley asking that the academy should arrange for a review of the facts relating to the genetic basis of intelligence. Shockley, who won the Nobel Prize for his work on transistors, has consistently tried to steer the academy into seeming to support his belief that blacks are genetically less intelligent than whites. He first tried to get the academy to sponsor a study of the genetic basis of intelligence as long ago as 1966, and in spite of being repeatedly snubbed by votes in the academy's meetings, he has been consistent in his efforts.

Shockley said last week that he introduced the motion at the spring business meeting because he believed that a report conducted by a special NAS committee under the chairmanship of Kingsley Davis had produced weak conclusions. He believes that the time is now ripe for the academy to produce a much more positive report, and presented evidence to the spring meeting to support his belief. His motion was, however, tabled because the paper containing his supporting evidence was presented two days after his motion, and members felt that they should hear his evidence first. Shockley will no doubt be at it again in April.

Surface Waves from Underground Explosions

SEVERAL authors[1,2] have published data on the surface wave magnitude (M_s) and yield (Y) for underground explosions at test sites in North America. Fig. 1 shows the dependence of M_s on yield for all test sites for which we could obtain explosion yield data. The details of the explosions are given in Table 1. From Fig. 1 it is clear that for explosions in consolidated rock (tuff, salt, granite, andesite and sandstone) all the observations lie close to the line

$$M_s = \log Y + 2.0$$

for yields from 4 kton to 1,300 kton. Only for Discus Thrower and Duryea does the observed value of M_s deviate by more than 0.3 magnitude units from this line, so only for these explosions would the yield estimated from M_s differ by more than a factor of 2 from the published yield. For explosions in unconsolidated rock (alluvium) the curve of M_s against yield seems to be more like

$$M_s = \log Y + 1.0$$

at least for yields less than 100 kton, but more data are required to define this curve. The M_s values plotted in Fig. 1 are means of individual station determinations of M_s, each of which is corrected for deviations of the source to receiver path from an average path. After correction, the standard deviation (SD) of an observation for a given explosion is usually 0.25 magnitude units and the SD on the mean value of M_s is about 0.1. Corrections are applied for the effect of the path on the propagation of surface waves of different periods. Over short paths in North America, for example, the large amplitude pulse-like arrival observed on wide-band long-period instruments is made up of period components close to a minimum value in the group velocity curve. This apparent large amplitude is due to the path and not to the source; the path effect can be estimated as a function of frequency and a correction determined (P. D. M. and P. Basham, to be published). It should be pointed out that path corrections are significant only for short transmission paths over which there is little dispersion. If these transmission path

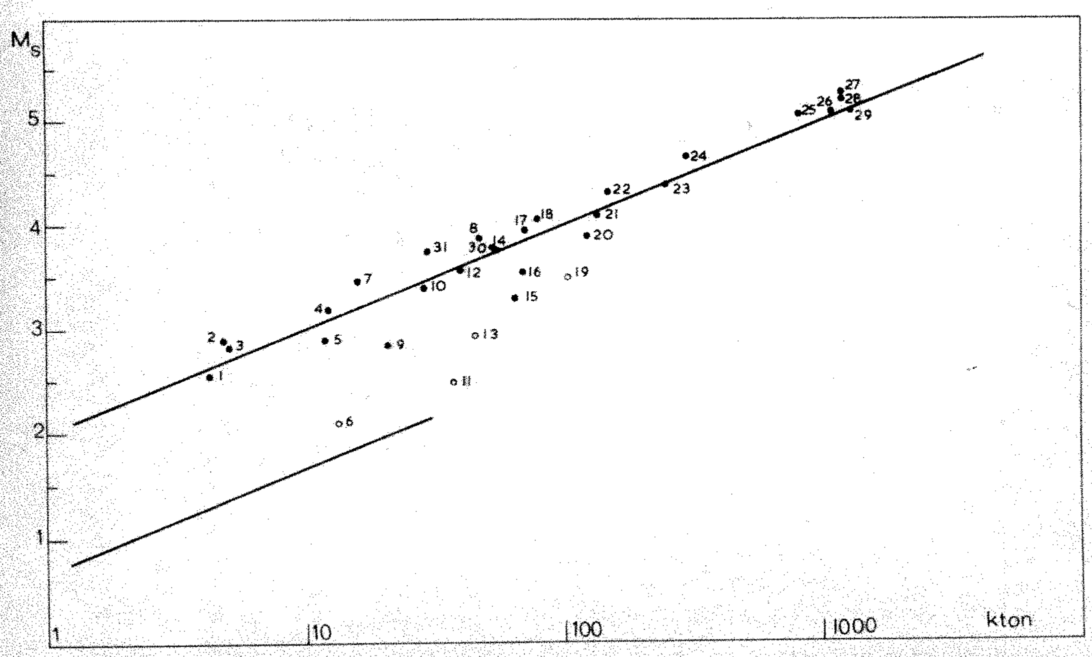


Fig. 1 Surface wave magnitude (M_s) against yield (kton) for explosions in various parts of the world.

Table 1 Details of Some Underground Explosions

Event No.	Date	Name	Region	Medium	Yield (kton)
1	April 14, 1965	Palanquin	Nevada	Rhyolite	4.3*
2	February 15, 1962	Hardhat	Nevada	Granite	4.8*
3	October 22, 1964	Salmon	Mississippi	Salt	5.3*
4	October 26, 1963	Shoal	Nevada	Granite	12.2*
5	November 5, 1964	Handcar	Nevada	Dolomite	12*
6	December 3, 1961	Fisher	Nevada	Alluvium	13.5*
7	February 24, 1966	Rex	Nevada	Tuff	16*
8	September 30, 1966	Bukhara I	Bukhara	Clay	30¶
9	May 27, 1966	Discus Thrower	Nevada	Tuff	21*
10	December 10, 1967	Gasbuggy	New Mexico	Shale	29*
11	October 9, 1964	Par	Nevada	Alluvium	38*
12	September 10, 1969	Rulison	Colorado	Shale	40*
13	June 27, 1962	Haymaker	Nevada	Alluvium	45.5*
14	June 2, 1966	Piledriver	Nevada	Granite	56*
15	April 14, 1966	Duryea	Nevada	Rhyolite	65*
16	May 6, 1966	Chartreuse	Nevada	Rhyolite	70*
17	May 26, 1967	Knicker Bocker	Nevada	Tuff	71*
18	October 29, 1965	Longshot	Aleutians	Andesite	85*
19	July 6, 1962	Sedan	Nevada	Alluvium	100†
20	January 15, 1965	Kazakh	Kazakh	Sandstone	125‡
21	February 27, 1965	Saphir	Algeria	Granite	135§
22	May 23, 1967	Scotch	Nevada	Tuff	150*
23	September 13, 1963	Bilby	Nevada	Tuff	250*
24	June 30, 1966	Half Beak	Nevada	Rhyolite	300*
25	December 20, 1966	Greeley	Nevada	Tuff	825*
26	December 19, 1968	Benham	Nevada	Tuff	1,100*
27	April 26, 1968	Box Car	Nevada	Tuff/Rhyolite	1,200*
28	October 2, 1969	Milrow	Aleutians	Lava	1,200‖
29	March 26, 1970	Handley	Nevada	Mesa	1,200‖
30	May 1, 1962	Beryl	Algeria	Granite	52**
31	May 21, 1968	Bukhara II	Bukhara	Salt	47¶

* Ref. 10; † *Vela "Uniform" Information Digest*, **2**, No. 11; ‡ inferred from *New Scientist*, May 19, 437 (1966) and ref. 13; § ref. 9; ‖ press reports; ¶ inferred from press reports and ref. 11; ** ref. 12.

corrections are not applied, the data do not display a consistent relationship between M_s and yield when data from different test sites are combined.

Theoretical curves of M_s against yield computed using the theory described by Hudson[3,4] and using the explosion source functions of Haskell[5] are also shown in Fig. 1. These theoretical computations have also been corrected to an average crust. For consolidated rocks, the fit of the computed curve with the observations is very good; for unconsolidated rocks the predicted value of M_s for a given yield seems to be rather low. (Theoretical predictions were only made up to 30 kton in unconsolidated rocks because this is approximately the maximum yield for containment in a surface layer of alluvium 0.5 km thick—the depth of the alluvium layer in the crustal model of the Nevada Test Site[6].)

From the data presented in Fig. 1 we conclude that, provided one assumes that explosions at any location have been fired in consolidated rock, yields can usually be estimated to within a factor of two. This is a great improvement on routine calculations using body wave magnitude. For example, the body wave magnitudes (m_b) of the MEDEO explosions (1.6 kton and 3.7 kton chemical explosions) were 5.0 and 5.2 respectively at Eskdalemuir (EKA)[7] whereas the value of m_b for the 40 kton Rulison explosion in Colorado was found to be 4.7 at EKA[8]. Fig. 1 also shows that the use of the $m_b : M_s$ criterion[9] to identify explosions at the teleseismic detection limit of $M_s \sim 2.5$ implies yields of about 40 kton in dry alluvium and 3 kton in consolidated rock. Long period arrays on low noise sites are required to record such low magnitudes at distances greater than 15 degrees from the firing site.

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NEWS AND VIEWS

Unravelling the Chromosome

JUST as the structure of DNA was the basic problem which had to be solved before molecular biology could become a meaningful discipline, so the structure of the eukaryotic chromosome is the vital issue which must be resolved before research today in cell biology can produce a coherent set of concepts instead of a mass of unrelated data. In his article on page 25 of this issue of *Nature*, Dr Francis Crick sets out his ideas on how DNA may be arranged in the chromosomes of higher organisms and what implications his model has for the control of the expression of eukaryotic genes.

The nub of his proposal is that the sites in eukaryotic DNA which are recognized by regulator molecules are not double stranded but comprise single stranded regions of unwound DNA. The nature of the regulator molecules which must interact with the control elements of DNA is unknown. But if they are RNAs, it makes obvious sense for the recognition sites to be single stranded regions of DNA with which complementary base pairing can take place. Because the active sites of proteins tend to be cavities within the molecules rather than protuberances out of them, it would also be easier for a protein regulator to recognize specific sequences of single stranded nucleic acids; the distinguishing groups on the base pairs of duplex DNA are located within grooves but are more readily accessible when the strands are unwound. (In bacteria, of course, proteins seem to manage to recognize specific sequences of duplex DNA.)

One of the most awkward facts to account for when analysing the heredity of higher organisms is their great excess of DNA; the amount varies with the species, of course, but there always seems to be far more DNA in the genetic material of eukaryotes than can be accounted for by adding up the number of genes needed to code for proteins. Dr Crick takes the line that the function of most of the DNA is to regulate the activity of the rest; compact "globular" DNA, which includes the unwound sequences, forms by far the greater fraction of chromosomal DNA—it is the more extended but much smaller fraction of "fibrous" DNA, taking up the conventional duplex structure, which codes for proteins.

What is the relationship of the control elements to the coding fractions? No matter what is the precise packing of DNA within the chromosome, it seems likely that it is one long molecule, running continuously from one terminus to the other. Sequences of control DNA will alternate with sequences of coding DNA. The manifestation of this model, Dr Crick proposes, is seen in the salivary glands of Diptera, which contain polytene chromosomes (made by a many-fold replication of the normal chromosome); under the microscope, large bands containing most of the DNA (the putative control elements) alternate with the much smaller interbands (the coding regions).

Why should so many regulators be needed to control the much smaller number of coding genes? There is no clear answer to be found for this question at present, but Dr Crick points out that the structures needed to maintain unpaired DNA cannot be constructed on too mean a basis. Another reason may be that a very precise quantitative control is required; it is unlikely to be sufficient just to switch genes on or off. Whenever a gene is to be expressed in some particular type of cell, therefore, its protein product may be synthesized to different extents. One control element might be needed for each type of cell in which the gene is to function.

To unwind DNA, of course, needs energy. Dr Crick points out that when large numbers of different control sequences need to be recognized it may nevertheless work out best to unwind the double helix before recognition. What unwinds the DNA? Dr Crick proposes that chromosomal proteins will achieve this and names the histones as his most likely candidates for the job. Unwinding might result from the formation of some complex structure in three dimensions, or instead it might perhaps be assisted by specific "unwindase" protein(s). The bacteriophage T4, of course, specifies as the product of its gene 32 a protein which seems to have the function of unwinding DNA for replication and recombination. Similar proteins probably assist meiosis in higher organisms; whether they are also present in somatic cells is an open question.

How do the regulator elements function? Dr Crick's model is compatible with either positive or negative control or both—RNA polymerases might recognize promoter-like sites or repressor molecules might recognize operator-like sites. What is the structure of the globular regions? Only some of their DNA will be unpaired; the conventional duplex segments could have a topological role or might perhaps be concerned with producing the regulator molecules themselves. Dr Crick does not say whether only the fibrous regions can be transcribed to RNA; the proportion of globular DNA is so great that it would be surprising if its only function were passively to be recognized. What are the proportions of regulator sites which comprise recognition elements and sites which code for regulator molecules is another unanswered question.

Dr Crick's article provides a chromosome structure to go with control models which suppose that each coding gene is accompanied by a long sequence of DNA concerned with regulating its functions; the best known model of this sort is, of course, that of Britten and Davidson. It will obviously be difficult to gather evidence either to support or to refute Dr Crick's model, but his prediction that globular regions contain single stranded DNA provides the most obvious handle with which to tackle the problem. And if chromosomes do prove to contain extensive amounts of single stranded DNA, models for the coiling of the nucleoprotein particle may need to be rethought.

As Dr Crick himself says, this model raises as many questions as it answers. It will nevertheless serve a valuable purpose if it focuses attention of cell biologists on the critical questions which need to be answered. Unhappily, it is not obvious how this will be done.

Water on the Moon and the Apollo Programme

SPACE enthusiasts must be regretting that the report of what may be molecules of water emanating from the surface of the Moon did not come sooner. It is much too late to save the two Apollo flights that were cut from the programme last year amid uproar from lunar scientists. And it is now unlikely that the second of the last two Apollo flights, Apollo 17, will also be docked from the programme, contrary to what the pessimists were saying a year ago. But the hypothetical water has surfaced just in time to participate in the debate on the need or otherwise to continue the exploration of the Moon after Apollo 17.

In these circumstances the announcement by Dr John Freeman of Rice University, Houston, was bound to be cheering news for the space zealots. To them, the approximately two pints of water which are estimated to have been responsible for the observations imply that the Moon may contain some of the basic raw materials that would have to be ferried there if a scientific colony is to be established. It remains to be seen, however, whether Dr Freeman and his colleagues are raising false hopes. The cloud of gas identified as containing water molecules was recognized in data obtained on March 7 by the suprathermal ion detectors left at the sites of the Apollo 12 and 14 landings. The cloud seems to have been triggered by a series of seismic events. But Dr Freeman is reported to have said that although water vapour is the most probable explanation of the readings, any of several less surprising gases such as ammonia, neon or other rare gases could also have been responsible.

On this basis it would be a mistake if the possibility of large amounts of water trapped beneath the lunar surface were to colour the exploration of the Moon in the same way as the possibility of living material on Mars has been a chief consideration in the design of planetary probes. For the present, the outcome of Freeman's announcement will be to focus attention on equipment to be carried on the Apollo 17 flight to examine the electrical properties of the surface layers of the Moon, which could conceivably reveal the layer of subsurface ice or water.

In the long term, however, it would also be risking disappointment to use the hypothetical water as an apologia for the continuation of lunar exploration after Apollo 17. While officials of NASA have been stumping the country for the support which they hope will prevent the shuttle programme from suffering the same fate that befell the supersonic transport, many scientists, inspired by the outcome of the Apollo programme, have been living in the hope of funds for a modest continuation of manned lunar exploration when the Skylab experiment is over in 1973. Even without the equivocal evidence for lunar water there should be no shortage of justifications for, say, the launch of a manned and heavily instrumented Apollo spacecraft into a polar orbit around the Moon.

The view that space research after 1973 should continue to concentrate on the Moon will not go unchallenged. Many people would rather first of all ensure that there is enough money in the scientific budget of NASA to follow up the amazing series of discoveries by the X-ray astronomy satellite. This is why the Space Board of the NAS has given priority to the automatic observatory carrying X-ray and γ-ray equipment and scheduled for launch in 1975, rather than to the Grand Tour probes to the outer planets. Indeed, there are signs that NASA has come to terms with the doubts that have been expressed about the Grand Tour, which also include the difficulty of constructing planetary probes that will have to be an order of magnitude more reliable than the present Mariner series. Studies are under way to see what could be salvaged from the Grand Tour project—once considered essential for NASA's well being in the late nineteen-seventies—if it has to be cancelled.

DNA REPLICATION

Restarting Replication of the Bacterial Chromosome

from our Cell Biology Correspondent

WHEN an episome such as the sex factor F, or a lysogenic bacteriophage, becomes integrated into a bacterial chromosome it is replicated passively along with the rest of the bacterial genome of which it is now part even though F factors and the genomes of lysogenic phages carry genetic determinants capable of controlling and initiating their own independent replication. Apparently these genes which function when the F factors or phages exist in an autonomous state become subordinated to their counterparts in the bacterial chromosome upon integration. But what happens when the phage or episome is integrated into the chromosome of a temperature sensitive mutant bacterium which is unable to initiate the replication of its genome at some nonpermissive temperature? Can the replication machinery of the episome or prophage as it were take over and initiate the replication of the entire bacterial chromosome? The answer to this intriguing question, no doubt much to the gratification of Jacob, Brenner and Cuzin, the postulators of the replicon theory, is that it can.

Earlier this year, Nishimura, Caro and Berg (*J. Mol. Biol.*, **55**, 441; 1971) reported that when an F factor integrates into the chromosome of CRT46 cells—a mutant strain of *Escherichia coli* which is unable to initiate the replication of its DNA at 42° C—the bacteria become Hfr and can replicate their DNA at this temperature. This "integrative suppression" by F factor of the temperature sensitive lesion in CRT46 cells indicates that the entire bacterial chromosome has in effect become part of the F factor replicon.

Now in the latest issue of the *Proceedings of the US National Academy of Sciences* (**68**, 2407; 1971), Lindahl, Hirota and Jacob report that the replication of the *E. coli* chromosome can come under the control of prophage P2 genomes. The Paris group, having found that P2 replicates in CRT46 cells at 42° C, and therefore has its own genetic machinery for initiating DNA replication, set about isolating mutants of this phage which by lysogenizing CRT46 cells can cause the cells to replicate at 42° C. Exploiting a strain of P2 known as $P2tsD_4c_5$, which specifies a temperature sensitive repressor and cannot complete its replication at 42° C because of a block in the maturation of phage tails, they obtained lysogens of CRT46 and selected for cells which would grow at 42° C. A few of the cells which survived this selection were found to liberate phage particles one strain of which was studied further.

This phage which suppresses the T46 mutation when it lysogenizes carries a third mutation, sig_5, which by three factor crosses has been mapped on the phage P2 genetic map and has been shown to be an insertion. This phage integrates at several sites in the *E. coli* chromosome and when it is at least one of these sites the T46 mutation is suppressed. Furthermore, in a series of elegant crosses Lindahl *et al.* have established that a protein specified by the gene *A* of P2 is required to suppress the T46 mutation and allow the cells to replicate their DNA at the nonpermissive temperature, 42° C. This A protein is probably essential for the initiation of DNA replication and biochemists eager to come to grips with this process would dearly like to get their hands on it. But it has one tantalizing property; it is a *cis* acting protein and probably cannot be investigated by any sort of complementation analysis because it only acts on the genome which specified it. The biochemistry of DNA replication retains its secrets.

MEMBRANES

CMF Controls Mg Flux

from our Membrane Correspondent

WHEN cytoplasmic macromolecular fraction (CMF) was first described by Loh *et al.* (*Biochemistry*, **7**, 726; 1968), it did not seem to be of more than passing interest, because it was only reported as affecting the oxygen consumption of dinitrophenol (DNP)-inhibited mitochondria. Later it transpired (Kun *et al.*, *ibid.*, **8**, 4443; 1969) that CMF also prevented the loss of magnesium ions from DNP-inhibited mitochondria. Binet, Gros and Volfin (*FEBS Lett.*, **17**, 193; 1971) and Binet and Volfin (*ibid.*, 197) now report significant progress towards the determination of the structure of CMF and ascribe to it a more universal role in membrane function.

CMF (now called cytoplasmic metabolic factor) in common with many substances of profound biological activity is present in tissues at very low concentrations. From 5 kg of porcine liver, Binet *et al.* eventually obtained 1.5 mg of CMF, but it was not possible to assay its purity because they were unable to get it to migrate in the thin-layer chromatography systems used. Their analytical results suggest that CMF is a water soluble, acidic cyclic peptide of twenty amino-acid residues, sixteen of them different. The water solubility and amino-acid composition indicate that there is little similarity between CMF and cyclic peptides such as gramicidin-S or alamethecin which can act as ionophores (that is, promote the transport of ions) in membranes. Indeed, the chief effect of CMF is to inhibit the movement of magnesium ions across membranes. Apart from confirming that CMF prevented the leakage of magnesium ions from mitochondria, Binet and Volfin also found that CMF prevented the light-induced ejection of magnesium ions from chloroplasts and inhibited the lethal ejection of magnesium ions from *Escherichia coli* which had been treated with the drug 'Levallorphan'. They also found that CMF promotes the uptake of calcium ions by sarcomes but unfortunately do not report whether CMF affects the transport of ions other than magnesium or calcium.

Thus the role of CMF is apparently to control magnesium and calcium fluxes across biological membranes. How it achieves this at the molecular level is at present unclear and is likely to remain so until more is known about ion transport mechanisms in membranes. CMF may prove, however, to be a useful tool in elucidating these mechanisms.

Magnetic Variations in Columnar Basalts

COLUMNAR basalts have seldom, if ever, been used for palaeomagnetic purposes, partly for the obvious reason that they occur only infrequently but partly because their peculiar structure induces the suspicion that directions of magnetization may be dependent on factors other than ancient field directions. This suspicion was largely confirmed by Symons (*Geophys. J.*, **12**, 473; 1967) from a very thorough study of a single column from the Giant's Causeway, Northern Ireland, which showed that not only palaeomagnetic properties but also inherent magnetic properties vary greatly throughout a column.

It seemed to Symons that the varying magnetic properties (natural remanence, Curie point, coercive force, bulk susceptibility, saturation magnetization and others) are essentially those which depend on the compositions of the titanomagnetites present and that such compositional variations as there are arise from differences in oxygen rather than from titanium content. And because such magnetic and compositional variations are likely to be the result of the unusual method of formation of columnar basalts, study of these variations could help to solve the vexed question of just what this method is.

Similar conclusions have now been reached by Radhakrishnamurty *et al.*, who in next Monday's *Nature Physical Science* report a study of some of the magnetic properties of columnar basalts from Bombay. Although, unlike the Giant's Causeway, little geological investigation has ever been made of these columns they are known to be hexagonal prisms of coarse-grained basalt about three feet across and up to more than 100 feet in height. No mineralogical variations from the centres to the edges are apparent in either thin or polished section, yet hysteresis loops in a field of 1,500 oersteds show that coercive force increases from the edge to the centre both at 25° C and −190° C. A similar variation of coercive force is found in samples previously heated to above their Curie points, although in each case the coercive force is significantly higher than in the corresponding virgin sample. Changes in the magnetic state clearly take place on heating; and curves of low field susceptibility against temperature show that these changes depend on the position of the relevant sample within a column.

Because in most cases the coercive force and saturation magnetization of virgin samples do not depend on temperature between 25° C and −190° C, Radhakrishnamurty and his colleagues conclude that the operative magnetic mineral is neither magnetite nor titanomagnetite. On the other hand, X-ray diffraction studies indicate the magnetic mineral to be "akin to magnetite". For the heated samples the hysteresis loops indicate the presence of magnetite (mostly) towards the edges of the columns but maghemite towards the centres.

These data, together with hysteresis loop comparisons with synthetic magnetites and maghemites, lead Radhakrishnamurty *et al.* to believe that the operative magnetic minerals in the virgin basaltic columns are intermediate phases in the magnetite–maghemite oxidation chain. To account for this the authors propose that although magnetite formed uniformly throughout the magma during initial cooling, and before columnar jointing, subsequent (radial) temperature gradients would lead to variations in the degree of oxidation within a column.

ION-MOLECULE REACTIONS

Precision Kinetics

from our Molecular Physics Correspondent

ONE of the most encouraging things about the present renaissance in chemical kinetics is the steady advance of both theory and experiment along lines which interconnect to a far greater degree than seemed possible ten years ago. While experimentalists are continually refining the accuracy with which the elementary reactive collision can be observed, theoreticians are beginning to grasp the nettle of calculating from quantum-mechanical principles the energy surfaces which must underlie any precise dynamical description of the sequence of events during a bimolecular encounter or a decomposition. One thing is important above all for this programme—the accumulation of reliable and precise data for reactions involving atoms and molecules with as few electrons as possible.

What is perhaps the most precise and thorough study ever made of a bimolecular reaction with small atoms has recently been completed at the Hahn-Meitner Institute in Berlin by Von G. Bosse, A. Ding and A. Hengelein (*Ber. Bunsenges.*, **75**, 413; 1971). The reaction concerned is the ion-molecule process

$$O_2^+ + D_2 \rightarrow O_2D^+ + D$$

The accuracy achieved required a skilful combination of the most refined techniques for beam generation, definition and product detection, which, until recently, were more likely to be reserved for an atomic physics experiment. The O_2^+ ions could be generated in both the $^4\pi_u$ and $^2\pi_g$ electronic states; they were accelerated into a collision chamber containing deuterium, beyond which the scattered reaction products could be analysed for both angular distribution and energy using a quadrupole mass spectrometer with 'Channeltron' detectors. A variety of striking results emerged.

As a preliminary, Bosse *et al.* show that reaction of $^2\pi_g$ O_2^+ sets in at a precise threshold energy (1.7 eV centre of mass) which corresponds closely to the independently calculated endothermicity of the reaction. This explicit demonstration of an activation energy — the fundamental experiment of chemical kinetics, in fact—would have been a sensational result in its own right not many years ago. The principal conclusions, however, are drawn from a series of energy-dependent scattering profiles obtained to quite unprecedented accuracy. Here the crucial feature is the presence or absence of isotropic scattering (centre of mass system) in the reactive-scattered beam of O_2D^+. This is now accepted as a sensitive indicator of the effective lifetime of a collision complex in a bimolecular encounter. Isotropic scattering arises where the lifetime is longer than or comparable with a rotation period; a "forward peak" in the scattering profile indicates a virtually instantaneous "stripping" mechanism for the process. By a peculiar quirk of the present reaction both possibilities can be observed in different energy ranges. With the $^2\pi_g$ O_2^+ ion there is a long-lived complex at low incident energies (17 to 40 eV laboratory system) giving way at higher energies to a stripping mechanism in which the O_2^+ ion seems to extract one deuterium atom with virtually no momentum transfer to the other one. With O_2^+ in the $^4\pi_u$ state, however, there is no sign of a long-lived complex at any energy, a finding almost certainly connected with the strong repulsion caused by the parallel alignment of spins in the recoiling products. Much additional information is also extracted concerning interaction cross-sections, isotope effects with HD rather than D_2, and the role of angular momentum. Significantly, almost all the heat of reaction in the exothermic $^4\pi_u$ reaction finds its way into translational energy of the fragments rather than into rotation.

There will certainly be much food for the theoretician in the results of Hengelein's group and a strong stimulus to the search for other interesting reactions of comparable simplicity. At the same time, in setting new standards for the precision possible in ion-molecule studies, the results confirm that it is likely to be many years before anything like this degree of detail is possible in the results of experiments with neutral beams, notwithstanding the great advances recently made with these.

Although on the theoretical side enormous difficulties remain before a reaction, even of this simplicity, can be treated *ab initio*, there is still a great deal which can be learned by semi-empirical and computer simulation methods. One of the most striking aspects of the present move towards fundamentals is the shift which has occurred over the years in the use of the term mechanism, particularly so far as bimolecular gas reactions are concerned. No longer does this denote simply the gross particulars of intermediate stages which can be written out in chemical formulae; the term has increasingly taken on the meaning of collision mechanism; that is to say, a reference to the subtleties of the collision complex itself, its formation, lifetime and mode of decay, the arrangement of energy in its different degrees of freedom. The elucidation of the

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Origin of Cosmic Rays

ALTHOUGH it is almost sixty years since Hess established the existence of cosmic rays the question of what fraction of the radiation, if any, comes from outside the galaxy is still unresolved. The Sun can on occasion produce charged particles with individual energies of up to 10^{10} eV. This energy overlaps the lower end of the cosmic ray energy spectrum in the region where most of the total energy resides, but the total output of this form of solar energy is very low and even if all other stars were as productive the observed cosmic ray energy density cannot be accounted for in this way. Because of this it is current fashion to think in terms of super novae explosions or pulsars as the principal generators of cosmic rays.

At the other end of the spectrum cosmic ray energies seem to go as high as 10^{19} to 10^{20} eV, if the interpretation of the large air showers is to be believed, and it has been customary to invoke an extra-galactic source for these super high energy particles because of the difficulty in finding sources with sufficiently high magnetic fields to accelerate them and because the interstellar magnetic fields are too weak to contain them within the galaxy.

Up to a few months ago the available picture of the general shape of the cosmic ray energy spectrum lent credence to a mixed galactic/metagalactic origin for the particles, but recent analyses of data from the large air shower array at Haverah Park have shown that the apparent decrease in slope of the spectrum above $\sim 10^{17}$ eV which was observed in earlier work at Volcano Ranch is almost certainly illusory. This change in slope had been attributed to a metagalactic cosmic ray flux.

In next Monday's *Nature Physical Science* F. W. Stecker re-examines the question of cosmic ray origin in the light of these results and of the interaction that should take place between ultra high energy metagalactic cosmic rays and the photons of the 2.7 K black-body radiation field. This interaction should lead to an upper energy limit to the cosmic ray spectrum and to a universal gamma-ray flux. Stecker considers several alternative cosmic ray models and concludes that the new spectral shape and the established upper limit to the gamma-ray flux are best explained in terms of a purely galactic origin for cosmic rays of even the highest energy. He offers only two alternatives; either the energy of air showers with $E \gtrsim 6 \times 10^{19}$ eV has been overestimated or there is no universal black-body radiation.

laws governing these details seems likely, not merely to provide an interesting chapter in chemical rate theory, but also to give firmer grounds for a claim that chemical reactive scattering is a subject worthy of the kind of attention which theoretical physicists have hitherto reserved for atomic and nuclear phenomena.

CANNABIS

Chemistry and Biology

from a Correspondent

Last week (October 26 to 28) the Swedish Academy of Pharmaceutical Sciences sponsored a symposium on the chemistry and biological activity of cannabis which was held in the Foresta Hotel on the island of Lidingö, near Stockholm. The wealth of detail presented in the thirty-five contributions left no doubt that very significant advances in knowledge have been made since a somewhat similar conference was held two years ago (*The Botany and Chemistry of Cannabis*, edit. by C. R. B. Joyce and S. H. Curry; Churchill, London, 1970).

Work on the metabolism of the active tetrahydrocannabinol (THC) is now well advanced. Shortly after administration this highly insoluble substance is metabolized to the more soluble 7-OH, 6,7 dihydroxy and even more soluble acidic derivatives and several routes to the synthesis of these compounds and their radioactive labelling are now known (R. Mechoulam; J. L. G. Nilsson; T. Petrizilka). The THC seems to be fixed to some of the plasma lipoproteins (H. A. Klausner; M. Widman) and to be rapidly transferred to the liver, spleen and the cortex of the adrenals (J. I. Heikkilä; Ryrfeldt J. Schou). Microsomal oxidation produces the more polar metabolites and they, and unchanged THC, are found in brain tissue shortly after administration (S. Agurell; S. Burstein; E. W. Gill). Correlation of concentrations in the brain with behavioural effects in small animals, primates and man has been established (M. E. Wall; M. Willinsky; W. M. McIsaac; E. A. Carlini; J. Hrbek) although it is still not certain whether THC or its metabolites are the active substance (W. D. M. Paton, who also pointed out the interesting connexion between fat soluble anaesthetics and the fat soluble THC).

A second impression was of the scientific complexity of the cannabis problem. The plant itself is a very plastic species with a large variation in the amounts of THC produced (J. W. Fairbairn). Apart from THC, another thirty related cannabinoids have been characterized and some of these may be active (F. W. H. M. Merkus; T. B. Vree) or may modify the total activity; for instance, cannabidiol (CBD) prolongs phenobarbitone sleeping time in mice (W. D. M. Paton). But P. Waser's suggestion that CBD is converted to THC on smoking was not generally accepted. Reports on the amount of THC surviving the smoking process gave results varying from 20 to 80 per cent, so that it was difficult to know whether a 5 mg, 10 mg or 20 mg THC content of a reefer would produce a "mind-rocking experience" or not. Even the nomenclature is confusing; sixteen contributions used the benzpyran system of numbering and thirteen contributions the terpinoid, so that one had continually to remember that Δ^1 and Δ^9, or 7-OH and 11-OH, were the same compounds. Steps are being taken to rectify this situation.

O. J. Braenden (Division of Narcotic Drugs, UN, Geneva) and M. C. Braude (National Institute of Mental Health, Rockville) described their ambitious programmes to coordinate effort and reduce overlap and confusion as much as possible.

A third important topic discussed by a panel, with the press present, was whether cannabis is harmful to health. Although definitive answers are not yet possible, it was interesting to note that, in the light of recent knowledge, nearly all the experts gave the impression they were against liberalization of use. The serious possibilities were raised of teratogenicity, tachycardia (especially if main-lining ever started), brain damage, accumulation in body fat, interference with microsomal enzymes (and therefore unknown effects on other drugs being taken for medicinal purposes), and carcinogenicity because deep inhalation is necessary for the full effect of a reefer. More general effects are a motivation leading to lack of drive and "dropping out", although N. E. Zinberg stated he had not noticed this markedly after a study of marihuana use in Vietnam. Unpleasant psychotic effects are also frequently reported and experimental work shows a slowing down of reaction time and inability to estimate time accurately; these effects can be serious when driving a car. Sir Harry Greenfield (International Narcotics Control Board) also pointed out that countries with a long history of cannabis use (for example, India, Egypt) are the most insistent on strict legal control.

A final impression gained was the hope that useful therapeutic substances may yet emerge and R. K. Razdan's work on crystalline water soluble derivatives of THC with interesting pharmacological properties may point the way. Abstracts only of each contribution will be published in *Acta Pharmaceutica Suecica*. Addresses of the speakers mentioned in this report may be obtained from *Nature* office.

Regulating the Initiation of Translation

The notion that initiation factors in *Escherichia coli*, by regulating the binding of ribosomes to specific "start translating" signals in messenger RNAs, regulate the expression of particular genes at the level of protein synthesis, receives further support in next Wednesday's *Nature New Biology*. Berissi, Graner and Revel, who have studied the effect of initiation factors F2 and F3 on the binding of *E. coli* ribosomes to the RNA of bacteriophage MS2, a close relative of R17, conclude that factor F3 selectively promotes the initiation of translation of the MS2 coat protein cistron.

The binding of ribosomes to MS2 RNA in its native configuration depends on the presence of two initiation factors, F2 and F3. If, however, the MS2 RNA is partially denatured by exposure to dilute formaldehyde, a procedure developed by Lodish, ribosomes will bind to the RNA in the absence of factor F3 although factor F2 is still required. This finding provided Berissi *et al.* with an opportunity to ask whether or not F3 is capable of promoting the specific attachment of ribosomes to one or more of the initiation signals on MS2 RNA. In essence all they had to do was compare the ratio of the number of sites on partially denatured MS2 RNA bound to and protected by ribosomes in the presence of F2 alone or F2 and F3.

The results of such experiments proved to be all that anybody could hope for. With factor F2 alone the ribosomes bind to the initiation sites of the coat protein, RNA replicase and maturation protein in the ratio of 1:2:1 but when factor F3 is also present, although the total number of ribosomes bound does not alter significantly, the ratio is shifted to 1:0.5:0.14. In other words factor F3 specifically promotes the recognition of and binding to the initiation signal at the beginning of the coat protein cistron at the expense of the other two cistrons; factor F3 promotes the expression of the coat protein cistron.

Berissi *et al.* have started to look for other F3 factors which might specifically promote the translation of other cistrons or sets of cistrons, for the idea that gene expression is regulated in part by a battery of different F3 factors is obviously most attractive. So far they have discovered one other F3 factor, called F3B4 to differentiate it from F3B2 which promotes the recognition of the MS2 coat protein cistron. F3B4 does not stimulate the attachment of ribosomes to MS2 RNA but it does stimulate translation of phage T4 messenger RNA; it will be no surprise if the list of specific F3 factors rapidly lengthens in the near future.

SELFASSEMBLY

Tricks with Ribosomes

from our Molecular Biology Correspondent

SINCE Nomura and his colleagues achieved the small miracle of mixing 16S RNA with its complement of some twenty ribosomal proteins to give active *Escherichia coli* 30S subunits, strenuous and hitherto unsuccessful attempts to reassemble the large subunit of the same species have been made in many laboratories. True, Nomura's group succeeded with 50S ribosomes from the thermophilic organism, *Bacillus stearothermophilus,* so that the principle has been in no doubt. Now, however, Maruta, Tsuchiya and Mizuno (*J. Mol. Biol.*, **61**, 123; 1971) have found the conditions for making active *E. coli* 50S subunits from their constituents, and more, regenerating the small and large subunit simultaneously in a single mixture of the three ribosomal RNA species and all the proteins —a process which may be compared to assembling a watch by putting all the parts in a bag and shaking.

The trick, so far as the 50S subunit is concerned, is to avoid exposure of the proteins to the solvents that are normally used for extraction and dispersion. Instead they are freed of RNA by treatment with nuclease. The native ribosomes are very resistant towards nucleases, but after partial unfolding in a medium containing molar ammonium chloride, the RNA becomes labile. When treated with the endogenous *E. coli* ribonuclease II, therefore, the RNA is hydrolysed to oligonucleotides, and the proteins are left, mostly as a precipitate, which will dissolve in a concentrated buffer solution. This is the protein preparation used in the reconstitution experiments, for if any attempt is made to remove nucleotide material by dialysis, no ribosomes can be regenerated. Evidently, therefore, some of the 50S ribosomal proteins are easily converted into a state from which specific interaction with the other ribosomal constituents becomes impossible. Bovine serum albumin is also included in the mixture as an obscurely beneficial component.

The reassembly reaction has a number of remarkable features. As with *B. stearothermophilus* ribosomes, the functional 50S subunit is not formed unless 30S subunits are present, or alternatively, as Maruta *et al.* now find, the mixture of the proteins and RNA of the 30S subunit. Moreover when only the proteins originating from either the 50S or 30S particle are labelled, all the label reappears in the right place after reassembly. That is to say none of the proteins from either subunit are captured by the other subunit, in spite of their basicity and the stupefying complexity of the system. The resulting ribosomes are active in poly U and viral RNA-dependent polypeptide synthesis. The 5S RNA which resides in the large subunit is indispensable for activity. It may be added separately, as a final step in the reconstitution process.

This last effect—the reversible release of 5S RNA from the 50S subunits—has been studied in other laboratories. Gormly, Yang and Horowitz (*Biochim. Biophys. Acta*, **247**, 80; 1971) have also used concentrated ammonium chloride at low magnesium concentrations to bring about a partial relaxation of the subunit to a more slowly sedimenting state. Liberated with the 5S RNA under these conditions are several ribosomal proteins, four species being completely and another three partially dissociated. On returning the ribosomes to their usual magnesium concentration, the 5S RNA is taken up, and folded subunits again appear. This process, however, also required the presence of the dissociated protein fraction —a conclusion apparently at odds with a report last year by Reynier and Monier. Unfortunately the restored ribosomes appeared not to be biologically active.

Gray and Monier (*FEBS Lett.*, **18**, 145; 1971) have tried another approach to identifying the ribosomal proteins directly associated with 5S RNA. They incubate 23S and 5S RNA with fractions of 50S ribosomal proteins and detect the formation of complexes by the membrane filtration method. A magnesium-dependent stable complex is indeed formed with one column fraction of 50S proteins. This complex can be isolated by sucrose gradient sedimentation, and when the proteins are analysed by gel electrophoresis three major and two minor zones can be resolved. One of the former is associated with 23S RNA even in the absence of 5S.

Infrared and the Black-body Background

SINCE the discovery by Penzias and Wilson (*Astrophys. J.*, **142**, 419; 1965) of 7 cm radio noise, thought to be remnant cosmological radiation with a black-body temperature of about 2.7 K, much attention has been paid to measuring the background radiation of the sky at wavelengths from the near infrared out to the radio region. Measurements which verify the possible existence of the background radiation have been made on the long wavelength side of the black-body peak, predicted to be at about 1.5 mm, but observations near the peak and at shorter wavelengths are not possible from the ground because of atmospheric absorption.

In recent years rockets have been used for investigating the sky background in the millimetre, sub-millimetre and infrared spectral regions from above the atmosphere. Two contributions on this topic appear in next Monday's *Nature Physical Science* and present conflicting measurements of the far-infrared background levels. D. P. McNutt, K. Shivanandan and P. D. Feldman report results of a recent Naval Research Laboratory flight in which they measured sky background in the 10 to 30 μm, 100 μm and 280 μm regions. A. G. Blair reports on rocket measurements obtained by the Los Alamos group in the 65 to 70 μm region.

The NRL experiment was launched on a Black Brandt VB rocket from Wallops Island on February 24, 1971, at 2013 EST and data were obtained between altitudes of 130 km and 275 km over a time period of 135 s. The photometer was cooled to a temperature of 2.8 K and the intensity calibration was estimated to be accurate to within a factor of two. Results indicated that at zenith angles less than 20°, scattered earthshine was unimportant, and the signal levels were interpreted in terms of a true background 100 μm radiance of 1.4×10^{-9} W cm^{-2} sr^{-1} and a 280 μm radiance of 2.9×10^{-9} W cm^{-2} sr^{-1}.

The Los Alamos experiment was launched from Kauai Test Range on May 29, 1971, at 0048 HST and carried a radiometer cooled with liquid helium to measure background fluxes in the spectral region 65 to 170 μm and 0.8 to 6.0 mm. The 0.8 to 6.0 mm results are not inconsistent with the proposed background 2.7 K black-body cosmic radiation. These results are discussed in a previous publication (*Phys. Rev. Lett.*, **27**, 1154; 1971). In the 65 to 170 μm region, Blair puts an upper limit of 1.2×10^{-10} W cm^{-2} sr^{-1} on the 100 μm radiance. This figure is consistent with previous results obtained by both the NRL group (*Science*, **167**, 1277; 1970) and the Cornell group (*Nature*, **281**, 375; 1971) but is more than an order of magnitude less than the current results of McNutt *et al.*

In looking for reasons to explain this large difference, McNutt *et al.* discard the possibility that they are detecting ionospheric radiation. Summarizing all rocket data available for the 100 μm and 280 μm regions, they conclude that those flights near local midnight show comparable low radiance levels whereas the earlier Cornell experiment (*Science*, **164**, 1271; 1969) and their current results—both recorded near astronomical twilight—are significantly higher. They suggest the possibility of a contribution from the outer magnetosphere, or near-Earth interplanetary space, which could be subject to a diurnal variability. They reject, however, the likelihood of a correlation between radiance and geomagnetic index K_p.

YEAST

Control of Budding

from our Microbiology Correspondent

With so much being written these days on the subject of morphogenesis and its biochemical foundations it is refreshing to come across a piece of work in which cellular differentiation has been resolved in some detail at the molecular level. Dr Enrico Cabib and his colleagues at the National Institutes of Health in Bethesda have been following a very simple morphogenetic event, that of budding in yeasts. Their latest findings (Cabib and Farkas, *Proc. US Nat. Acad. Sci.*, **68**, 2052; 1971) bring together the details of a chitin synthesizing system which is responsible for initiating septum formation between the mother and daughter cells. The specificity both of timing and localizing this event seems to be produced by conversion of a chitin synthetase zymogen to the active enzyme by an activating factor (AF).

Earlier this year, Cabib and Bowers (*J. Biol. Chem.*, **246**, 157; 1971) had confirmed previous reports that chitin is concentrated in a disk-like plug from which the bud has detached. They have now shown that chitin synthesis occurs in a stepwise fashion in synchronized populations of *Saccharomyces carlsbergensis*. Similarly the chitin synthetase of *Saccharomyces* species which was described as a particulate enzyme (Keller and Cabib, *J. Biol. Chem.*, **246**, 160; 1971) is revealed to be largely in an inactive or zymogen form which can be activated about 15-fold by treatment with trypsin. The endogenous AF can be recovered in high-speed supernatants of the sonicated enzyme preparations. Although the details of the AF have not been elucidated, it probably catalyses a specific proteolysis of the zymogen. Cabib believes that the enzyme is firmly bound to a particulate cell fraction whereas AF is enclosed in more fragile vesicles.

The nature of the synthesizing system is still more complex. A heat stable protein was discovered in the cytoplasm which was thought to be an allosteric inhibitor of the enzyme (Cabib and Keller, *J. Biol. Chem.*, **246**, 167; 1971). But further work has confirmed that the inhibitor interacts with AF and not with the enzyme *per se*.

In order to explain the triggering of chitin synthesis at a precise time and site, Cabib and Farkas offer the following hypothesis. Because chitin synthetase is largely in a zymogen state and the amount of it in the cell is surprisingly constant, it is presumed to be uniformly distributed in some structural component of the cell, most probably the plasma membrane. Following bud formation, AF-containing vesicles might fuse with the plasma membrane at the site of septation resulting in enzyme activation of chitin synthesis. Indeed, the presence of vesicular material at bud sites has been observed several times in yeasts. The role of the inhibitor is more enigmatic. One possibility is that it may serve as a safety device to immobilize AF that might be released into the cytoplasm and thereby prevent any indiscriminate enzyme activation and subsequent chitin formation. Experimental testing of this elegant model doubtless will be made in the near future and news of its veracity and generality will be eagerly awaited.

MICROSCOPY

Cryoultramicrotomy

from a Correspondent

A meeting and workshop on cryoultramicrotomy was held in Paris on October 18 and 19 and was the second meeting on specialized techniques in microscopy organized jointly by the Royal Microscopical Society and the Société Française de Microscope Electronique.

Dr W. Bernhard (Institut de Recherches Scientifique sur le Cancer, Villejuif) opened the session by reviewing the problems posed by cryoultramicrotomy, and showed that by carefully applying the technique to material which had been lightly fixed it was now possible to obtain morphological information from specimens equal to that obtained by more conventional techniques of embedding and thin sectioning. This excellent introduction to the meeting was followed by a series of contributions by commercial representatives on the physical principles of cryoultramicrotomes. No major advances in instrumentation were described, but all the speakers in this session stressed the importance of accurate temperature control of both the knife and specimen, and the necessity of a dry atmosphere in the cutting area.

The remainder of the first day was taken up by descriptions of some biological applications of the cryoultramicrotome. Dr L. Seveus (LKB, Stockholm) and Dr G. Werner (Saarlandes University) showed that fixed material, frozen, thin sectioned and then dried at low temperature, can give the same type of image obtained by more conventional means, although membranes can only be seen in negative contrast. Organelles such as mitochondria, although recognizable in unfixed material, rarely show internal membranes. Dr T. Appleton (University of Cambridge) gave several useful hints for the handling of frozen sections, and for drying the sections at low temperatures. He also showed that ultracellular membranes in unfixed material seem to appear as an array of linear dots, and said that the interpretation of morphological data obtained by cryoultramicrotomy should not be based solely on the usual appearance of these structures in the electron microscope. Dr L. Paavola and Professor A. K. Christenson (Temple University) showed how necessary it is to work with unfixed material in studies of steroid synthesis in mammalian tissue.

On the second day, Dr S. Hodson and Dr J. Marshall (Institute of Ophthalmology, London) showed that even if sectioning is carried out at −180° C there is still likely to be some danger of surface melting of the specimen. Their studies showed that although this melting is considerably diminished in very thin section, it might seriously jeopardize high resolution localization of diffusable substances. The session continued with a paper on sectioning single cells and a discussion on whether it is really necessary to encapsulate the specimens before freezing. Dr A. Viron (Laboratoire de Biologie de Végétale, Orsay) and Dr S. Halpern (Institut de Recherches Scientifique sur le Cancer, Villejuif) described some results following cryoultramicrotomy of plant material, and it became clear that the watery vacuole of mature plant cells still presents a considerable barrier to successful cryosectioning of plant tissues. There then followed an exhaustive round table discussion which included contributions by Professor H. Moor (Technische Hochschule, Zurich), Dr P. Echlin (University of Cambridge) and Dr M. Grund (Reichert, Berlin) on some of the theoretical problems associated with rapid freezing. It was shown that the present techniques preserve adequately only the surface layers of specimens unless the samples are thoroughly soaked in cryoprotective agents. In many future applications of cryoultramicrotomy the use of fixatives and anti-freeze agents may not be practicable, and several new techniques were discussed including the high pressure method proposed by Professor Moor.

The afternoon session dealt with the application of cytochemical method and autoradiography to cryoultramicrotome sections. Dr Appleton showed that it was possible to localize by X-ray microanalysis ions and electrolytes in frozen dried sections, and Dr R. Simard (University of Sherbrooke) demonstrated the rapid loss from the tissue of diffusable substrates in material which had been fixed before freezing and sectioning.

In summing up this most stimulating meeting, Dr Bernhard agreed that the cryomicrotome has proved itself capable of providing morphological information, but said that its use should now be directed to providing thin sections of undisturbed biological tissue for analysis by the sophisticated techniques of histochemistry, autoradiography, immunochemistry and X-ray microanalysis.

Conflicts of Loyalty in Science

Although there is a traditional view that the chief duty of scientists is to the scientific community, their employment by government, industry or even universities may frequently impose other loyalties. At a symposium held on September 7, 1971, at the annual meeting in Swansea of the British Association for the Advancement of Science, an attempt was made to help to define the line that must be drawn between one loyalty and another. This article brings together the contributions to the symposium by Dr K. Mellanby, Mr Terence Price and Dr J. R. Ravetz.

K. MELLANBY

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BEFORE considering the scientist's responsibilities, we need to know a little more about him. Is there such a thing as "a scientist", someone who differs from the rest of humanity? Is the term now more or less obsolete and can we explain the difficulties of the British Association for the Advancement of Science by saying that "science" is no longer the distinct and meaningful term it once was? I think we must consider this carefully, because the layman still thinks of a scientist as a polymath, a person who can speak expertly on any scientific subject. Unfortunately some so-called scientists also make the same mistake, and pretend to give an informed and scientific judgment on subjects in which they themselves are laymen. They are disloyal to science.

To some, a scientist (particularly a research worker) is a glamorous figure, making epoch-making discoveries at frequent intervals. His work is considered important. If he works on the right subject, he will benefit mankind immeasurably, but if he studies the wrong topic, he will do untold harm. This picture is, of course, generally false. Most scientific research may add slightly to the body of knowledge, but most of it has almost no practical significance. It adds a few bricks to the edifice of knowledge, or a sliver of mortar. Most scientists are, in fact, profoundly unimportant.

This unimportance is accentuated by the fact that many scientists, even in universities where they have a considerable degree of freedom in the choice of their research subjects, seem to have a genius for selecting the trivial and avoiding the significant. Those who control research policy and those who direct other scientists are equally inept. But spotting the significant topic is not an easy matter and the elitist, academic approach to research—to work on a subject which may seem interesting and to damn its practical importance—may sometimes produce the best and most valuable results, even results useful to the technologist.

Thus last year, at the meeting of the British Association, Dame Honor Fell gave an outstanding presidential address to section D (zoology). She showed how practical results of great medical importance arose from the work of scientists working in different laboratories over a period of almost a hundred years; none of the work was aimed at its ultimate target.

The seemingly important subject may also disappoint. Until recently biologists have been impressed by the immense significance to mankind of molecular biology, and participants in this research have, deservedly, received a galaxy of Nobel laureateships. Now Sir Macfarlane Burnet states, with some authority, that all this brilliant work has made no contribution of any significance to medicine; he is even convinced that it never will.

There is also an interesting situation in ecology. We have been told that real progress will come from two directions, ecological energetics and computer-aided systems analysis. In the long run this may be true, but I have my doubts; I think that the practical value of this work is limited. At the same time we constantly hear that field studies are "mere natural history", a waste of time and energy, an unnecessary muddying of our ecological gum boots. We now know that just these studies, this natural history, has provided us with the most delicate tool for the early recognition of environmental pollution—and it is no accident that most of the members of the Royal Commission on Environmental Pollution are biologists, including at least three with extensive experience of just this sort of ecological field work.

Thus it appears that, although it is the responsibility of the scientist to wish to work in the field where his results will be of most value to science and mankind, the selection of this field may not be easy. The results are seldom those expected at the start of the work—if they were, then the work would not be really necessary! We should not, however, scorn the short-term *ad hoc* work, clearly intended to solve a practical problem. It seldom does so, but in the hands of good research workers, it often reveals unexpected and fundamental truths.

Scientists today may play an important part in giving advice to governments or to the public; this they have a duty to do. Unfortunately others cannot always distinguish the genuine from the bogus. A scientist may be the unique authority in his own speciality, but he is also a layman outside that field. If he allows himself to be considered an expert when he is not, he is a fraud and disloyal to science as a whole. We often come across these bogus experts nowadays, particularly in the realms of ecology, of pollution, and of pesticides. Let them remember that they are not polymaths, and keep their allegedly expert comments to their own restricted speciality. This does not mean that a scientist cannot speak out on all sorts of other matters, political and sociological, but he does this as an ordinary citizen and not as any sort of expert.

Knowledge is universal, and scientists have a duty to make their findings available to all. I would accept that someone employed in industry must, for a time, keep technical details of industrial processes secret and those who object are objecting to our capitalist system, not to something fundamental to science. I also accept that someone working in a military establishment must abide by the rules he accepts when he enters that sort of employment. Many may also object to this—the objection here is a legitimate political one, it is the advocacy of pacifism, and again the objection is not fundamentally a scientific one. With these possible exceptions, I believe that it is the duty of a scientist to make his work known and to give his expert advice whenever possible. Unfortunately there are cases where he may be prevented from so doing. A scientific civil servant does accept some limitations on his liberty, but these should be enforced as little as possible. I believe our authorities have quite a good record in this connexion, though I have, as editor of the scientific journal *Environmental Pollution*, known scientists in government laboratories to be forbidden to publish information, which cannot possibly be considered as affecting national security, for the administrative convenience of their minister. What is particularly objectionable is that the minister himself may know nothing about the prohibition, made in his name by some comparatively junior civil servant.

A scientist in a research council must never be so muzzled. Since the research councils were put under the Department of Education and Science, there has been a tendency for scientists to be told they must behave like civil servants and must not say or do anything which might "embarrass their minister". This is dangerous, and could lead to a situation where the only real experts, not the bogus ones who so often hit the headlines, are prevented from speaking—for in some subjects all the principal workers are employed in some way by government.

TERENCE PRICE

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I HAVE been asked to say something about conflicts of loyalty as they might concern someone with a broadly scientific or technical background who works at a fairly senior level for the government. In one sense this is a relatively easy task, because no one can reasonably ask me to resolve such conflicts once and for all. The point is that the work of government is precisely about conflict, and to assume that in a better-ordered world these conflicts might in some way be avoided is to ignore the obvious truth—that if any issues were so easily resolved they would have been settled lower down, without reaching the government level at all. Government cannot avoid dealing with that residue which defies orderly treatment. And because there is this conflict of policies, and because—fortunately—it is still men and not machines who engage in the final arguments, we must expect a similar conflict of loyalties to be only a step away.

The first point I would make is that many kinds of people, many professions and many interests necessarily have to contribute to these discussions. Science is only one voice amongst many. But it has one very important claim to a place at the top table: it is by far the largest inducer of change that the world has ever known.

This, of course, does not always make for the easiest professional relationships between scientists and their non-scientific colleagues. Science in a sense progresses blindly. It does only what it can. In the process it is continually creating problems, and there is nothing in the scientific method that guarantees that it will also provide solutions. Nothing could be further from the precepts of tidy administration. The man in Whitehall may not always know best (and in any case he is much too experienced to make such a claim) but he does know instinctively that some brake must be set on the rate of change if all is not to dissolve in chaos. His experience leads him to distrust men who claim that this or that project will, at a stroke, bypass some existing difficulty and lead us automatically into a better world. He sets more store by the words of Francis Bacon: "It were good therefore that men in their innovations would follow the example of time itself, which indeed innovateth greatly, but quietly, and by degrees scarce to be perceived; for otherwise, he that is hurt takes it for a wrong, and imputeth it to the author". And again: "Those things which have long gone together are confederate within themselves, whereas new things piece not so well". We are not dealing with a new phenomenon. It is only the scale that has changed.

But in changing the scale we have created a new source of conflict between science (and I am using the word to include technology) and all the other claimants on national resources. Generally speaking—as Sir Alec Cairncross stressed at the beginning of this conference—the growth of science has not, in practice, been matched by any very convincing relevance to the needs of the national economy, nor by any explicit commitment to social objectives. Our promises as scientists were listened to with attention during the fifties, and if we had got things right this might still have been the case. But too much went wrong with atomic energy policy, and a king's ransom was squandered on cancelled aircraft. We never had it so good, and we shall never be allowed to have it so good again. If this leads us—indeed forces us—to be more objective about our own personal projects, it will, I think, be no bad thing. In the long run it may well be better to have doubts before the event about (say) the noise pattern which a city centre VTOL airport would create, than to pretend that its impact would be minimal.

But such doubts will not make running a large organization any easier. Large projects, like the VTOL city-centre aircraft of my example, can only come together successfully and on time if there is a unity of purpose in the execution, and an ability to enthuse the team with a belief in the rightness of their task. The Americans talk of "missions"—a well-chosen word with exactly the right quality to fire the zealot hidden in every man. But sophisticated doubts about mission objectives can create very personal conflicts for the mission leaders, particularly if they are also men who operate at a high level in the national context. In such a capacity they have to make judgments about the overall national good. But their entitlement to make such judgments springs from their position as spokesmen for large technical organizations, in which role they are expected to prevail in argument and to bring home the bacon in the shape of a fat allocation of resources. Here is a potential conflict which is usually inescapable. Not everyone finds it easy to resolve. Indeed, not everyone makes the attempt. The much vaunted objectivity or self-discipline of science applies, in fact, only to the actual process of observing or interpreting natural phenomena. There is not much evidence to suggest that this objectivity spills over into the wider social context.

In practice an administration defends itself against project leaders' more extravagant claims—not always very successfully, it is true—by taking some of these poachers and turning them into gamekeepers. Hence those shadowy teams of "neutrals" in places like the Cabinet Office. The conflicts of a neutral are more subtle. Lacking the support staff who would be needed to work up a view in the same detail as those who are putting forward a programme for expenditure, he usually has to make do with scanty information, and relies a good deal on hunches. He runs the risk of falling into the danger of pretending to a degree of detailed knowledge which he does not possess. Or he may become a persistent critic: all policies can be faulted, and it is easier to destroy than rebuild. The persistent critic eventually wears thin the patience of his colleagues, like a compulsive litigant. By squandering his resources he paralyses his ability to intervene on the really important issues. Most men are alive to this danger, and do not chance their arm too frequently. But there is then the possibility that they will be led into keeping silence at a time when it is necessary to speak out. "Don't rock the boat" can be a very effective curb.

When to break with established policy and take one's stand is indeed a terribly hard thing to judge. Once the move has been made it is irreversible. It is unwise to be wrong—particularly if, as can happen, you find yourself wishing to challenge the policies of some other sector of the organization. It is all too easy to be deterred by that other war-cry: "No influence with responsibility". Nevertheless challenges are made—though it is as well for the challenger to be equipped with adequate standing or adroitness.

At this point I can imagine someone saying—and indeed this was said earlier in this conference—that things would be so much easier, and there would be so many fewer conflicts, if only the government allowed its professional staffs to carry out their analyses of social and economic return in greater depth, and in more explicitly numerical form. To which the only possible answer is fiddlesticks. I have seen at first hand the workings of a large government group devoted to operational analysis. It tackled some largish issues and, I believe, made a useful contribution. But this did not automatically lead to a Utopia in which there were no conflicts—it simply shifted the point of contention to a different part of the decision chain. Herman Bondi once said: "If I find one of my students who has reached an answer with which I disagree, I never look at his mathematics. His arithmetic is always right. I look at the assumptions which precede equation one."

It does not take anyone who has suffered from an unwelcome conclusion of an operational analysis study—and has come near to losing his own project as a result—to learn this lesson: he ripostes by attacking the assumptions. Moreover, this kind of analysis is a game that two can play, and once a fashion for decision by analysis has developed it is not too difficult for a skilful staff to decide on the desired outcome, and then to construct an analysis which will point in that direction. Nor is this necessarily wrong. Debate is a good thing and out of it may, perhaps, come truth. My point is that it is naive to hope that by any purely technical approach these conflicts and debates can be avoided. They cannot, because they are fundamental. And in any case numbers can be a terrible straitjacket. As Denis Healey once remarked: "Don't just give me facts that can be expressed in numbers. I also want facts that can only be expressed in words."

Anyone who has read Parkinson, or Snow—or even Solzhenitsyn—will recognize these conflicts as those of any organization man. And you may wonder that I give them so much prominence, where others might have preferred a discussion of more meaty issues, like biological warfare. The fact is that I have not, in my own experience, found that these have led to a personal conflict of loyalties, whereas the others are there with you (and all other organization men) all the time, each time you enter your office.

I can, of course, well imagine that the conflicts posed by Porton or Aldermaston are real enough for those who work there; but I was fortunate in having to deal with such issues only at several removes, and I have no quarrel with the way in which I was allowed to work out my own thinking. Indeed, in relation to the political and military problems posed by the existence of nuclear weapons, I can only regard the attitudes of my own immediate colleagues as enlightened. One of the problems was the effect of the development of atomic energy on disarmament policy. The point was taken early on that there were limitations on the extent to which fissile material could be tracked down, and thus on the degree to which it would be safe to reduce both nuclear and non-nuclear armaments. Total nuclear disarmament was therefore a non-starter. But some attitude had to be taken by the government, and we were privately encouraged to clear our minds on what, if anything, might still be possible. We took part in the disarmament conversations at London and Geneva, and were encouraged to go if we wished as observers to Pugwash, or to participate in private meetings of bodies like the Institute of Strategic Studies. There was no intellectual conflict here—it was the problems that were difficult. The more one became acquainted with the issues, the less one felt able to share the certainty of the Aldermaston marchers, admirable though they were as people. And yet they were not wholly without influence: it may have been partly due to their conviction that something ought to be done that it was possible to have a serious, and on the whole reasonably convincing, discussion within Whitehall. Whatever the reasons, I personally never felt myself under pressure to subscribe to a doctrine in which I did not believe.

What I did sometimes regret was the inability to communicate this feeling to the public at large. The inhibitions about publication, already mentioned by other speakers in this discussion, naturally loom very large in such a field. This stems to some extent, here and elsewhere, from the constitutional doctrine that only the minister is permitted to enunciate policy. One cannot help feeling, with government activities as widespread as they are today, that this doctrine is perhaps in need of some overhaul.

It may be relevant that the intellectually satisfying atmosphere that I am describing occurred during a period when the Ministry of Defence had at its head (under the minister) three very remarkable men—one of whom had only recently come in from outside the civil service. The place of irregulars in Whitehall is a favourite battle-ground, and I certainly do not wish to adopt a doctrinaire attitude. Some of the importations have not worked, and only rather exceptional men have learnt to take their place in such a complicated machine, and to be really effective. Nevertheless one could be forgiven for doubting whether a government service that was wholly inbred would always be capable of creating the atmosphere of intellectual stimulation that I was fortunate enough to experience. The irregular has an essential function to perform. And even for him it will not always be easy.

In case I seem to be straying too far from the subject, let me say that the link in my mind is the question of how we are to handle the really central issues. These are what tear men apart unless they are dealt with effectively. Anyone who has sat through the meetings of the British Association knows that problems are going to increase, in intensity and in number, as the human race learns to live in balance with the rest of this small planet. In the process, we shall have to develop a new basis for economics and a new orientation for technology. Even the moral basis for our policies may come increasingly into question. All this, to my mind, underlines the need for the changes that are now beginning to take place—too slowly, perhaps—in the structure of the government service. If they mature, they should go some way towards minimizing the danger of inbreeding, and should avoid at least some of the conflicts which could occur if the government machine failed to keep up with change in the world outside.

I will end with three thoughts. First, there is the need to recognize the perennial nature of the conflicts which we face. Only the subject matter, and perhaps the pace, are new. The methods by which they will ultimately be resolved—with more or less elegance, depending on the participants and the luck of the draw—will be those on which the human race has always had to rely: argument, persuasion and decision. If scientists are dissatisfied with the way in which the great issues are tackled, by all means let them go and try their hands at doing better—but only after due preparation. The requirements for success in the world of affairs, or (to use Lord Zuckerman's telling phrase) for effectiveness at the point of action, are what they always were—you can find all you need in the essays of Francis Bacon from whom I quoted earlier. Do not make the mistake of thinking that the sociology of a government department equates with that of a laboratory or a university. They have very little in common. Second, the institutions within which the conflicts are resolved are very relevant; they deserve the closest attention. Third, the quality of argument within the government machine is often encouragingly, even outstandingly, good. Some of the fears which exist might well be removed if the arguments could be made more easily available to the general public.

J. R. RAVETZ

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I FEEL that I must challenge the assumptions on which our discussion is based. May I call your attention to the opening clause of the statement of the scope of the session: "Scientists are brought up to believe that their chief duty is to the scientific community . . .'. I am sure that to the organizers of the session, this was obvious common sense. But we live in an age when common sense becomes obsolete with increasing speed, and the common sense of the social activity of science is no exception. For this statement is an assertion about a state of affairs among a particular social group: advanced students of science. As such, it may be true or it may be false; or it may be that it was true yesterday but will be false tomorrow. Whatever its degree of correspondence to the social reality of science, this can be determined only by a study of evidence concerning that social reality. And on balance the evidence indicates that it is no longer true.

I am not raising this objection merely to be difficult; there are two important points concerned with it. The first is that this statement belongs to a field of enquiry that can be called "the sociology of science". The field is small and fragmented; and it is possible that reflective scientists can offer more insights to it than those who approach science from the outside. On the other hand, its problems are not those of research science and, in this field as in any other, pitfalls abound for those who are overly confident in their common sense understanding of its phenomena and problems.

It is true that until recently sociologists of science accepted and reinforced the common sense view that neophyte scientists are inculcated with a sense of duty to their scientific community. But as soon as serious empirical studies began to be conducted, this common sense was exposed as a myth, at least as regards the situation today. Here I refer you to the writings of Box and Cotgrove, Ernest Rudd, Norman Ellis and Barry Barnes. So my first point is that scientists who engage in the laudable and necessary work of discussing the social problems of science would do well to remember that even when discussing themselves, as members of a group, they are amateurs.

The second point is more serious. For if, as I maintain, the common sense view about this important aspect of science is no longer true, then there is a two-fold consequence; the social activity of science has suffered an important change in recent times and the common sense of some leading scientists has not yet caught up with it. In that case, the discussion of "duties" and "loyalties" among the units of scientific manpower, or QSEs as they were labelled not long ago, is only partially relevant to the social problems of science at the present time.

This is not to say that conflicts of loyalties are now insignificant for the life of science. They are there but I shall argue that the most important foci of conflict are no longer those around traditional professional groupings and roles. For these have become attenuated and, at the same time, some other, very deep problems have become recognized. I will try to identify these new conflicts of loyalty in terms of the new social character of science.

A clue to the change in science is provided by the term "the scientific community". The last word, much overworked nowadays, bears with it connotations of what the sociologists call *Gemeinschaft*: a group held together by stable, direct, interpersonal relationships. By the end of the past century, social philosophers recognized that this type of society was rapidly being extinguished in Europe and being supplanted by one they called *Gesellschaft* where the relationships are essentially impersonal and the ties are contractual and formal.

We have long been familiar with the distinction between "little science" and "big science" and it seems to me that the implied change in scale carries with it very deep consequences for the character of the social activity of science, along the lines of the change from *Gemeinschaft* to *Gesellschaft*. I have described elsewhere the difference as one between the "academic science" of the recent past, and the industrialized science" of the present. By industrialized I do not merely mean that science has come to be considered primarily as a factor in production when it is being planned. And the capital-intensive character of research makes inevitable a concentration of decision-making power and a differentiation of scientists into groups analogous to social classes, where the many are dependent on the decisions of the powerful few. Also the supposed economies of excellence of scale among the social units of production lead to a concentration of research, and even more of research training, in favoured large centres. These conditions are very different from the earlier state of largely independent individual scientist-craftsmen, each being able to accommodate only a few apprentices and being sufficiently small and poor a community to be bound by personal ties and governed by largely informal means.

With such a drastic change in the social character of scientific research, we must expect significant changes in its more subtle ideological aspects. To be brief, the graduating scientist finds the best job he can; he does not join a profession and still less does he take up a vocation. This is my impression, based on talks with young scientists, and I am supported by scholarly social investigation. For this generation of recruits, conflicts of loyalties of the traditional sort are usually absent.

I can agree that the problems referred to in the statement of the scope of our session are real ones; I would only prefer to describe them as problems of responsibility. For the scientist working in a university, nominally in a "pure" field, they can be severe and, on occasion, destructive. For the university man's job includes several roles including that of teacher, social worker, administrator and researcher. We are all aware how the progress of his career within institutions performing these multiple functions is determined largely by his prowess as a researcher which is assessed by networks of colleagues that operate across and outside such institutions. The recent American experience of student revolts shows what happens when the conflicts inherent in that situation are not controlled. For there the great universities, or multi-versities, had degenerated into unstable collections of research baronies. Faced with crises affecting them as institutions, they were paralysed. To describe the cause of this as a conflict of loyalties is to miss the point entirely; for it was the total absence of loyalty of the big scientists to their universities that made them so vulnerable. In this country our crises are never so severe, for many reasons; yet it would be naive to assume that our scientists, and their students, have somehow retained intact the good old-fashioned virtues.

The political aspects of the most recent American student challenges indicate some conflicts of responsibility that naturally lead to considerations of loyalty. For there has arisen a conflict of responsibilities, roles and images, when university scientists, nominally "pure" and independent scholars, actually function as technicians on mission-oriented research. This contradictory situation leads to strains on the scientist's job. There is the delicacy of secret research (whose secrecy may also be a secret!) and there is a likelihood of the distortion of the criteria by which problems are chosen for research students. But most serious, there is an inducement to self-deception or hypocrisy, where the scientist sincerely claims the privileges and immunities appropriate to a member of a community of scholars (as in the indignant rejection of the idea that his university has anything to do with politics, while unself-consciously enjoying the power and material benefits accruing to him as a partner in industrial or military enterprise).

At this point we can truly speak of conflicts of loyalty, at least for those scientists who are not complete opportunists. To be sure, there is no simple opposition of loyalties here, between (say) national patriotism and the ideals of university scholarship. But never again, after the war-science scandals at American universities, will it be possible for scientists to assume that whatever is good for the Department (or Ministry) of Defence is good for their university. To the extent that a university scientist has loyalties with objects both within and without his institution, he will need to recognize genuine potential conflicts between them.

On the problem of conflicting loyalties of this sort, we are indebted to Professor Ernst Chain for providing us with the limiting cases, as it were, of possible solutions. His recent television performance dealt with a restricted case; those scientists who, in a democratic society, voluntarily become soldier-technicians. He believes that they thereby contract a lifelong obligation of obedience to their organization, otherwise they become "traitors". Apparently he would deny such scientists the rights and demands of conscience that an ordinary soldier has under the Nuremberg Code of war crimes. Sir Ernst's earlier essay was more bold and perhaps more consistent. There he asserted that the scientist's social responsibility entails a completely subservient loyalty to his employer and/or government. But there he did not mention political ideals as proper objects of loyalty, so we must conclude that a scientist under a Soviet or Nazi regime should obey his masters similarly. Also, in the absence of any assurance to the contrary, we must assume that Professor Chain's scientist may not challenge the state in its definition of goals and problems of science. I find it difficult, therefore, to see grounds on which Lysenko would legitimately be opposed. And as a *reductio ad absurdum* of this position, one may question whether collecting specimens for Himmler's "anthropological" museum of *Untermenschen* was not a war crime but, by definition, a scientific exercise.

Of course such things could never happen here and so perhaps Professor Chain should not be required to follow his speculations to their possible logical conclusions. But even our democratic military technology can lead scientists to quite serious conflicts of loyalty. An example, discussed at the BSSRS teach-in at Durham last year, is the campaign of American computer experts against the proposed anti-ballistic missile system. They could see, and demonstrate, that such a system could not possibly operate to the standards of precision and reliability necessary for it, but the Pentagon did not want to know. So as a last resort, they took the law into their own hands and denounced the ABM system publicly. What loyalties impelled them to this extreme and potentially dangerous step? As "professionals" they could have derived great profit from a long and expensive series of fruitless attempts to improve this among other specious weapons systems. It must, therefore, have been loyalty to their own personal integrity to stop a particularly blatant bogus project and also to the human race, to prevent a "mistake".

I believe that, in such a case, there are genuine problems of conflict of loyalty in contemporary, industrialized science. Assuming the veracity of Goffman and Tamplin, they had just such a conflict when the Atomic Energy Commission told them to bring Sternglass's estimates of pre-natal deaths from fallout from several hundred thousand to absolute zero. It is possible that similar conflicts presented themselves to the scientists tasting the dangers of the insecticide dichlorvos in Vapona strips.

Such conflicts of loyalty involve very generalized and diffuse objects and principles and the scientific evidence on which they are based is frequently inconclusive. Hence they are inevitably controversial and—dare I say it—political. But it would be mistaken, and damaging, to regret their existence and to frame codes of practice under which they could not occur. For they represent the emergence of a new scientific conscience, and a new style of science, in response to the social conditions and social problems of industrialized science and science-based technology.

"Critical science" as practised by Linus Pauling, Rachel Carson, Barry Commoner, and the independent section of the environmental scientists, is the live and growing point of science today. Its members are doing for ourselves what the *Philosophes* of the Enlightenment did two centuries ago: exposing in detail and in principle the sterile and dehumanized common sense in which our present science and technology are conceived. To this movement, we are already indebted for the exposure of the institutionalized psychopathology of nuclear deterrence, the biochemical rape of Vietnam, the technomaniacs's obsession with bigger and faster means of transport, and the manifold pollution from "socially significant chemicals". At the fundamental level, it questions the identification of novelty with progress and makes us think again what science and technology are for.

Such work is fraught with difficulties and hazards. The ongoing work of society is done by specialists within institutions and so the critical scientist will always be needing to take food from the hand he is biting. Thus he will suffer correspondingly from conflicts of loyalty. But such scientists, who I believe are a small but rapidly growing minority among the units of the scientific-technical manpower pool, have a definite focus for their basic loyalties: to humanity, as stewards for nature. The conflicts they will inevitably experience can be creative, for themselves, for science and for us all.

R365

Cretaceous Seafloor Spreading in the Western North Atlantic

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Magnetic profiles parallel to and between fracture zones in the Cretaceous western Atlantic suggest at least twenty-five reversals between 135 and 90 m.y. BP, with a long normal period between 80 and 90 m.y. BP. The fracture zones constrain the position of the America–Africa pole.

In 1968 a geomagnetic reversal time scale corresponding essentially to Tertiary and Quaternary time (77 to 0 m.y. BP) was proposed, based on magnetic anomalies imprinted on the oceanic basement by axial accretion at the Mid-Oceanic Ridge[1]. For the period 5 to 0 m.y. BP, the reversal chronology has been calibrated against measurements of age and polarity made on rock specimens[2], and the portion of the reversal chronology[1] before 5 m.y. BP was later corroborated by the JOIDES deep sea drilling programme in the South Atlantic[3] and the other oceans. The uncertainties in the absolute age of reversals that occurred in the middle, or lower, part of the reversal chronology are probably no more than a few m.y., and the length of a particular normal or reversed period is probably known to an accuracy of about 0.1 m.y.[4]. Several slightly different reversal chronologies for post-10 m.y. BP time have been proposed[5].

There are several reasons why extensions of the reversal chronology to Mesozoic or still older ocean floor that may be present have been slow in coming. Although about two-thirds of the ocean floor is Cainozoic, deep sea drilling dates suggest that the oldest oceanic crust dates from at least 180 m.y. BP. Therefore, 55% or more of the surviving magnetic reversal time scale is located in a third of the ocean. This oldest third is also rather deep, covered with more sediment, and more densely studded with seamounts, making it difficult to delineate the magnetic anomaly pattern and deduce a reversal chronology from it. Another factor is that the later Cretaceous seemed to have been a time of predominantly normal polarity[6], producing little in the way of identifiable anomalies.

The first pre-Cainozoic reversal chronology was derived from a 300 km wide band of correlatable anomalies between 20° N and 45° N in the western Atlantic[7]. The correlatable anomaly train was named after the survey platform, USNS Keathley.

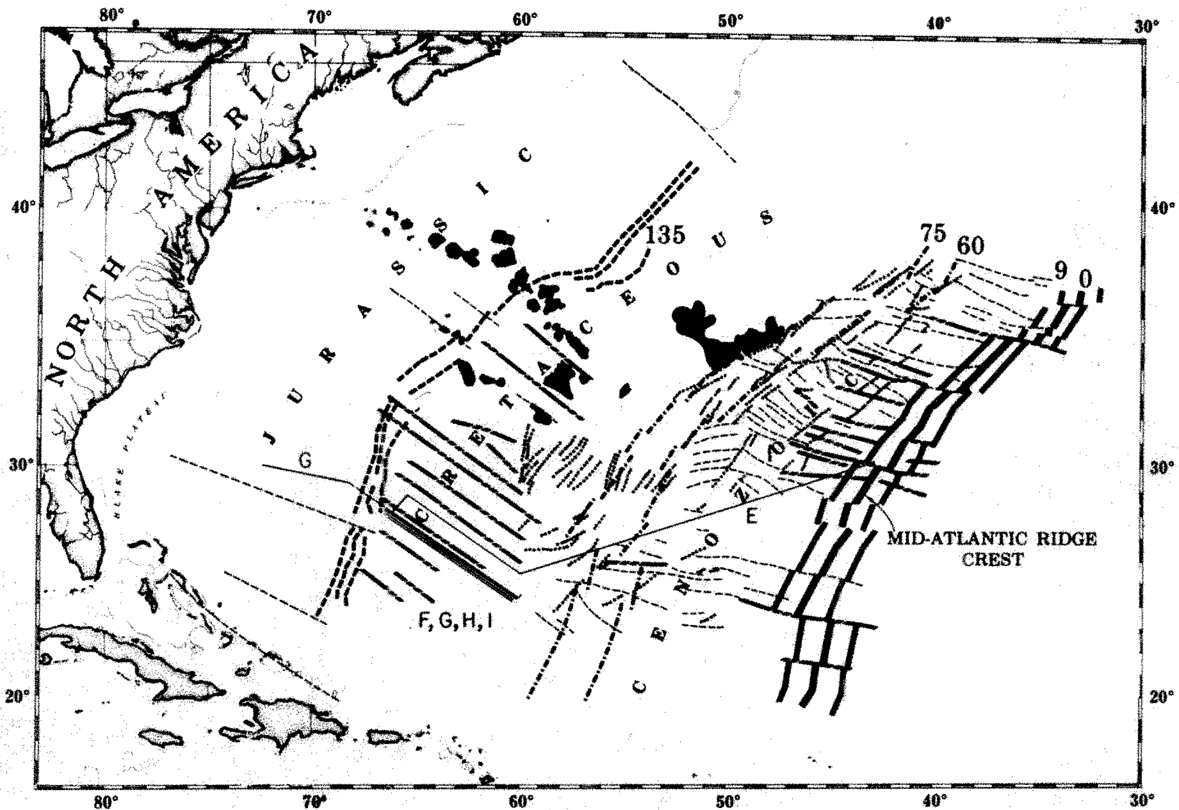

Fig. 1 Profile positions, superimposed on compilation of major isochrons, magnetic anomalies, and physiographic trends in the western North Atlantic[17]. Systematic surveying at 20 mile line spacing did not extend east of 60° W. Tracks are keyed to Figs. 2 and 3.

This "Keathley sequence" probably exists in the eastern Atlantic (although neither in the South Atlantic nor north of the Azores) and in the western Pacific[7]. From JOIDES drilling[8] the Keathley sequence was generated between 155 and 135 m.y. BP, with the mean reversal rate[7] close to the post-42 m.y. BP value[1] of 3 per million years.

The oldest Atlantic seafloor is represented by magnetic smooth zones about 500 km wide, lying between the Keathley sequence and the continental shelves west of North Africa and east of the United States. Extrapolation of JOIDES dates suggests the smooth zones were formed between 180 and 155 m.y. BP[8]. A preliminary study suggests that correlatable low amplitude (±30 gammas) magnetic lineations exist in the magnetic smooth zone[9]. If these reflect geomagnetic reversals, the reversal rate for that period must have been of the same order as for the period 155 to 135 m.y. BP.

Cretaceous Reversal Anomaly Pattern

One of the least known parts of the post-180 m.y. BP geomagnetic reversal chronology is the time between the Keathley sequence[7] (155 to 135 m.y. BP) and the Heirtzler time scale (77 to 0 m.y. BP)[1]. In this article we offer several well oriented magnetic profiles to fill the whole of what is approximately Cretaceous time.

A detailed bathymetric-magnetic survey of the western North Atlantic[7,10] revealed the Cretaceous crust east of the Keathley sequence to be densely fractured (Fig. 1). From the east–west tracks spaced 20 miles apart, and from other sounding data, fracture zones spaced about 100 km apart and trending N60W were identified (Fig. 2). Most of these fracture zones were apparently formed about 135 m.y. BP, a time of major spreading change in the North Atlantic, and probably the beginning of spreading in the South Atlantic[7].

The paucity of fracture zones on the Keathley crust made it possible to correlate the anomalies, but by contrast, the east–west magnetic profiles across the post-Keathley seafloor showed uncorrelatable anomalies[7]. The numerous fracture zones (Figs. 1 and 2) help explain why no pattern emerged.

During the summer and autumn of 1970, however, it was possible, aboard USNS Lynch, to search for a Cretaceous reversal sequence, because the position and trend of fracture zones were by then known. Closely spaced and accurately navigated lines (Fig. 2) were run parallel to and between two prominent fracture zones in an area of relatively smooth basement. An additional line was placed one crustal block further north to determine whether possible anomalies correlate across a fracture zone (as they should, if they are due to reversals) and whether any such anomalies are offset across the fracture zone, presumed to be a transform fault.

The residual profiles are shown stacked from north to south in Fig. 3. A correlatable magnetic signature is strongly suggested, and we have confidently numbered the more prominent anomalies of this "Lynch sequence" as K-1, K-2 and so on, the K prefix standing for Cretaceous. This is in keeping with the anomaly prefix J for the Keathley sequence[7], which is Jurassic in age[8]. We recommend the anomalies in the Heirtzler sequence[1] be assigned a prefix C for Cainozoic. The number scheme within both K and J sequences is in keeping with the precedent of Heirtzler *et al.*[1] in that numbers increase from youngest to oldest.

The K-anomaly correlations are tentatively shown in Fig. 3. Many more profiles will be required to identify all correlatable features. In particular, the oldest K-anomalies appear erratic, and we know the basement to be rough there. Thus, there is considerable doubt about the contribution made to the anomalies by magnetized basement relief. We intend to elaborate on this later (work to be published by P. R. Vogt and G. L. Johnson), when a model for the K-anomalies will be given. The middle K-anomalies are typical of reversal anomalies, and the basement under them is surprisingly smooth. At the young end, the relation to the Heirtzler anomaly sequence is still uncertain, as the fracture pattern east of 60° W is poorly known and the profile of Fig. 3 is oblique to the anomaly strike and probably cuts at least one fracture zone. The smooth zone between K-1 and K-2, however, apparently correlates with anomaly "R" identified just north of the Antilles[7]. This was evidently a long period of normal

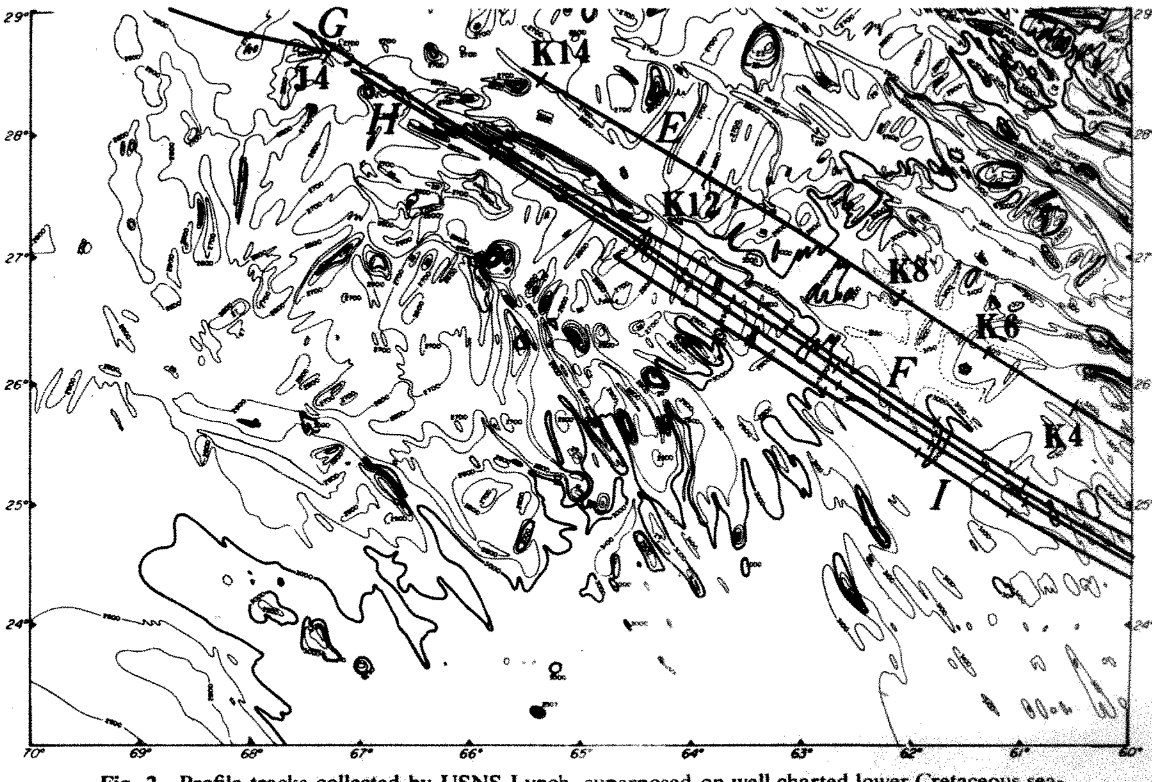

Fig. 2 Profile tracks collected by USNS Lynch, superposed on well charted lower Cretaceous seafloor on east flank of Bermuda Rise. Bathymetry from Johnson and Vogt[10]. Tracks and correlated anomalies are keyed to Fig. 3.

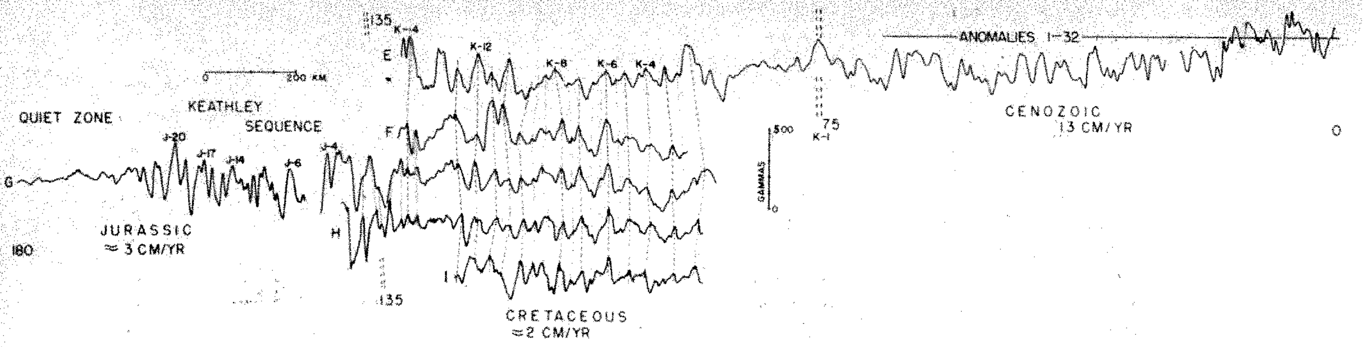

Fig. 3 Residual total field magnetic profiles. Suggested correlations that are more obvious are dashed and lesser features, possibly also correlatable, are dotted. Cretaceous (K) Lynch sequence is flanked by upper Jurassic Keathley sequence (J)[7] and well known Cainozoic anomalies[1].

polarity in the Upper Cretaceous[6]. If our identification is correct, K-1 and the smooth zone west of it (Fig. 3) may be identical to anomaly 33, a long period of normal polarity reportedly found in the Atlantic and Pacific basins[11]. Based on JOIDES drilling and extrapolations from Cainozoic anomalies, the long normal period lasted from about 90 to 80 m.y. BP.

The existence of numerous correlatable anomalies in the Cretaceous North Atlantic seems to conflict with the rather uniform Cretaceous smooth zone, indicating few or no reversals, reportedly found in the South Atlantic[12]. We agree that polarity was constant between magnetic highs K-1 and K-2, and possibly also between K-13 and K-14 (Fig. 3). These periods however, represent only a fraction of the Cretaceous. Unless South Atlantic lineations were subsequently erased (or our lineations are not the result of reversals), we have no explanations for this disagreement. If the Cretaceous were largely free of reversals, anomalies might still be created by variations in dipole intensity, but the anomalies should then be found in the South Atlantic also. Furthermore, a South Atlantic magnetic smooth zone of Cretaceous age cannot be due to spreading at equatorial latitudes. Another unlikely alternative is that variations in layer thickness or axial demagnetization produced the K-anomalies shown in Fig. 3. A more reasonable explanation, perhaps, is that anomalies K-2 through K-14 never gained respectable amplitudes in the South Atlantic because the early rift axis was kept inundated by sediment. Such conditions should inhibit the formation of a rapidly cooled, highly magnetized pillow lava layer. This explanation was invoked as a possibility for the older North Atlantic smooth zones[13].

In summary we feel confident that the K-anomalies shown in Fig. 3 represent geomagnetic reversals occurring during Cretaceous time. Neglecting the long normal period between about 90 and 80 m.y. BP, we conclude that at least twenty-six reversals, represented by 13 positive anomalies, occurred between 135 and 90 m.y. BP. This suggests a reversal rate of greater than 0.6 per million years. If the minor anomalous features, shown dotted in Fig. 3, are also interpreted as due to reversals, the reversal rate for the period 135 to 90 m.y. BP would have been close to 1 per million years, that is, about the same as for the period 77 to 42 m.y. BP[1]. It seems certain, however, that the 135 to 90 m.y. BP reversal rate was lower than the 155 to 135 m.y. BP and 42 to 0 m.y. BP values.

The results above conflict somewhat with land-based palaeomagnetic measurements from the Cretaceous, described by Helsley and Steiner[6]. The rock sample data show the Cretaceous to be predominantly normal, with the exception of two reversed intervals in the Maestrichtian (70–60 m.y. BP), one in the Santonian (78 m.y. BP), one at the Albian–Aptian boundary (110 m.y. BP) and two in the Neocomian (130–140 m.y. BP). The absence of known reversals between 109 and 77 m.y. BP and between 129 and 102 m.y. BP (all ages being interpolated from the data of Helsley and Steiner[6]) contradicts the anomaly data of Fig. 3. Possibly the zone between anomalies K-13 and K-14 corresponds to the later part of the 129 to 102 m.y. BP normal intervals, but there is still a serious overabundance of measured normal polarities, compared with the anomaly data. There are two ways to resolve this: (1) palaeomagnetic sampling in the Cretaceous has been severaly non-random, skewed toward normal intervals; or (2) the observed anomalies are due in large measure to basement structures or geomagnetic intensity fluctuations. We prefer the first explanation.

America–Africa Plate Rotation Pole during Cretaceous

The bathymetry of what JOIDES drilling suggests to be seafloor of Lower and Middle Cretaceous time (Fig. 2) is now

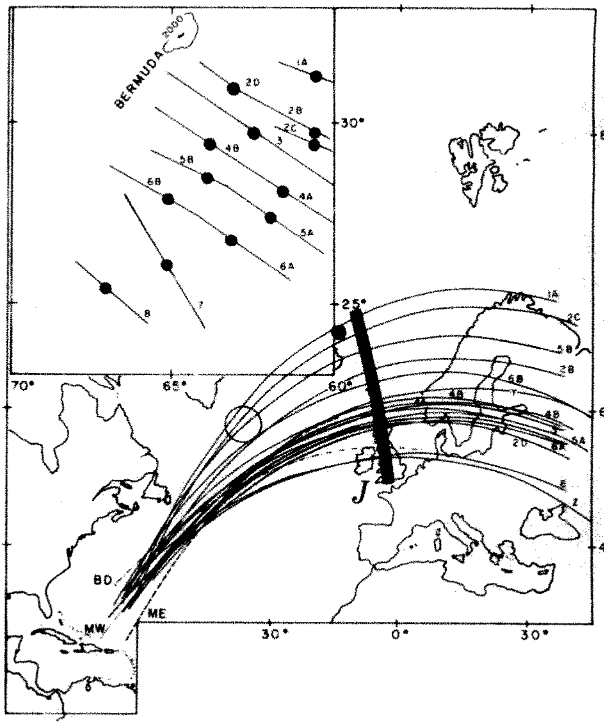

Fig. 4 Great circles normal to Cretaceous fracture zones (Figs. 1 and 2) clearly miss the late Tertiary America–Africa pole[16], shown as open circle, and the net or total opening pole, shown as filled circle[15]. BD is a fracture zone extending into the younger Keathley crust near Bermuda. MW and ME are magnetic anomalies probably associated with fracture zones about 100 km north of the Puerto Rico Trench[14]. Preferred pole is in shaded region, but even this is far from certain. Arc labelled J applies to Jurassic Keathley sequence; its intersection with great circles would give the virtual pole if the pole position did not change from Jurassic to Cretaceous.

charted with sufficient accuracy to disclose the positions and trends of major fracture zones[10]. In all likelihood, the fracture zones are transform faults, and therefore form portions of small circles described about the virtual plate rotation pole for the Cretaceous western Atlantic. To locate this pole, we constructed great circles normal to most of the fracture zones, in some cases at several points along a single fault (Fig. 4). We also interpret the linear south-east trending magnetic anomalies north of Puerto Rico[14] as lying along fracture zones. The great circles lie along a well defined band, but the position of the pole, somewhere along the band, is uncertain. The rate of northward narrowing of the K-anomalies (Fig. 1) will resolve this problem when it becomes known. In any case, it is clear from Fig. 4 that the pole coincides neither with the net Africa–America pole[15] nor with the later Tertiary pole[16].

In conclusion, five carefully oriented magnetic profiles suggest at least twenty-six geomagnetic reversals recorded as magnetic reversals on the lower and middle Cretaceous (135 to 90 m.y. BP) seafloor of the western North Atlantic. With less certainty, a long normal period occurred between 90 and 80 m.y. BP. Fracture zones give a good great circle azimuth to the 135–90 m.y. BP America–Africa virtual plate rotation pole, but the pole position along that azimuth remains uncertain.

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General Model for the Chromosomes of Higher Organisms

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The model suggests that chromosomal DNA falls into two classes: globular DNA (containing unpaired regions for control) and a much smaller fraction consisting of fibrous DNA which alone codes for proteins.

I WISH to propose a general model for the structure of the chromosomes of higher organisms*. This model is derived from ideas and data from many sources†. Because I have found it impossible to set out my ideas and the supporting evidence in a short space, I merely summarize here my conclusions. A much fuller account is in preparation and will be submitted for publication in the near future.

The model assumes that the DNA in a chromatid is a very long mononeme (see the review by Prescott[2] and the recent careful work by Laird[3]), which probably runs continuously from one end of the chromatid to the other.

The model has three basic features. (1) The coding sequences of the DNA (that is, all those sequences which code for polypeptide chains) are postulated to be mainly, if not entirely, in the interbands (as visualized in the giant polytene chromosomes of the Diptera[4]). The bands, which contain all but a few per cent of the DNA, are identified as the control elements. This is illustrated diagrammatically in Fig. 1. A genetic complementation group is usually contained in a band plus an interband.

Thus on this view most of the DNA in higher organisms does not code for proteins but is used for control purposes, as already suggested by F. Vogel[6] in 1964. I have calculated that the average‡ amount of DNA (per mononeme) in an interband of *Drosophila*[7,8] is enough to code for an "average" protein of molecular weight 30,000–40,000. I have, therefore, adopted this speculation as a good working hypothesis.

(2) The central idea is that the recognition sites, needed for control purposes in higher organisms, are mainly unpaired single stranded stretches of double stranded DNA. I call this the Unpairing Postulate and it is set out diagrammatically in Fig. 2. It has been derived from a theoretical consideration of the general nature of protein molecules and the probable variety and length of the base sequences which need to be recognized in higher organisms. A particular type of example of this postulate has already been put forward by Gierer[9].

The argument I give is a general one. It springs from the

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* I have used the term higher organisms rather than eukaryotes because I want to avoid having to discuss, at this stage, the chromosomes of various lower eukaryotes such as the dinoflagellates and the fungi.

† Proper acknowledgments will be given in the fuller paper, but I cannot refrain from mentioning here the very stimulating theoretical paper by R. J. Britten and E. H. Davidson[1], which the reader is strongly recommended to read in parallel with this one. It contains extensive references to the earlier literature.

‡ The average amount of DNA in the mononeme of an interband had been estimated previously by Beermann[4].

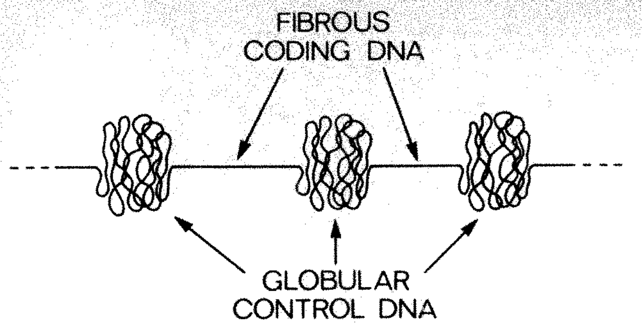

Fig. 1 An extremely schematic drawing of the proposed general structure of the DNA of the chromatid. The line represents part of the continuous DNA molecule in the mononemic chromatid. The straight portions correspond to the interband regions of the giant polytene chromosomes of the Diptera, which are postulated to be similar in their general character to the corresponding interphase chromatids, which are the active form. The mitotic chromosome is relatively inert[5]. The DNA sequences coding for protein are postulated to be mainly, if not entirely, in these extended regions. For convenience this DNA is referred to as fibrous DNA. The intricately folded regions correspond to the bands seen in the polytene chromosome[4,7]. No attempt has been made to represent their detailed structure. They are postulated to be the sites of the control regions. The model implies that a genetic complementation group is usually contained in either an interband plus a band or an interband plus part of the bands on either side. When a gene is active the bands are probably at least partly unfolded[4]. The globular DNA is certainly complexed with chromosomal proteins[10], the fibrous DNA probably so. Thus both should be more strictly referred to as nucleoprotein.

fact that for all proteins whose tertiary structure is known, the active site is, to a first approximation, a shallow groove or a cavity and not a protruding piece of the protein structure. The former structures can rather easily be made to provide highly specific interactions, both with small molecules or with extended polymers. However, in double-helical nucleic acid the specific groups on the bases are not protruding but are themselves in one or other of the two grooves formed by the phosphate–sugar backbones. Thus, it might not be easy to design a protein of reasonable size to recognize more than a limited number of base pairs, especially when one remembers the twisted nature of the normal double helix. The postulate has even more force if single stranded RNA is also used to recognize the control sequences on the DNA, as favoured (with reservations) by Britten and Davidson[1].

My argument is that when very large numbers of different sequences need to be recognized (which implies that the sequences must not be too short), it will pay to unwind the double helix before recognition. This may be expensive to arrange but in the long run it will provide a much greater abundance of versatility.

(3) The forces and energy needed to unpair the recognition stretches of the DNA are provided by the combination of the DNA with chromosomal proteins—probably the histones[10]. Although the three-dimensional configuration of a band may be very intricate, such globular structures may be based on structural motifs of various kinds. The most obvious one is a simple supercoiled DNA, that is, a helical double helix, as already suggested by various workers[11,12], but other more complicated structures are possible[11]. One such example is illustrated in Fig. 3. As far as I know this suggestion is a novel one.

The general property of this family of structures is that there are lengths (probably of hundreds of base pairs) of DNA whose exact base sequence matters very little, interspersed with shorter stretches (perhaps of a hundred bases or so) of specific sequences which are probably repeated at very many places along the DNA. On this view the role of the histones is not merely to cover up the DNA but to help the DNA to expose itself in the right places.

Plausible general reasons can be given why the bands (the control elements) are so large compared with the interbands (the coding elements). In the first place, the type of structural motif outlined in Fig. 3 cannot be constructed on too small a scale. Moreover, as Britten and Davidson[1] have pointed out in their Fig. 1*A*, multiple control elements may well be needed adjacent to each particular coding sequence. In addition, a set of similar elements may be required within certain bands to help provide a graded response. Finally, it appears to be a general rule that intricate three-dimensional biological structures are always bigger than one might naively expect. The examples of globular proteins, transfer RNA and ribosomes spring to mind.

My fuller paper will discuss possible mechanisms for the formation during evolution of these large control regions. It would seem likely that both tandem repetition and translocation will be involved. Whatever the origin of tandemly replicated sequences (satellite DNA[13] or otherwise), when they are first formed there will be an exact repeat of the sequences both in the paired region (such as the stem of Fig. 3) and in the regions which become unpaired (such as the loop of Fig. 3). However, during evolution, mutations will accumulate at different rates in these different regions. The paired regions will diverge rapidly, since the exact base sequences there do not matter appreciably, but changes in the unpaired regions will occur less rapidly, if at all, because they have to interact with other molecules during control operations. Thus, newly evolved bands (or parts of bands) would be expected to have a closer degree of tandem repetition of their base sequences than phylogenetically older ones.

The model, in its simplest form, suggests that the number of different proteins normally produced by higher organisms may not be much more than a few thousand for *Drosophila* and

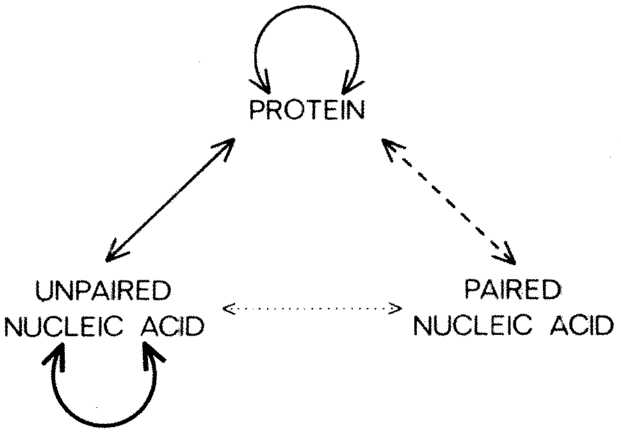

Fig. 2 Each line represents the possibility of a highly specific interaction between two macromolecules. One molecule is from the class at one end of the double arrow and the other is from the class at the other end. Notice that no distinction is made between RNA and DNA. Instead, a strong distinction is made between paired nucleic acid (meaning a stretch of double helix) and unpaired nucleic acid which can be either single stranded nucleic acid or unwound stretches of an originally double helical structure. The latter may or may not be refolded to some extent into three-dimensional structures having a complex mixture of paired and unpaired regions[9] such as is found in transfer RNA. The dotted line represents the formation of a triple helix, such as poly A + 2 poly U. The dashed line represents the recognition by a specific protein molecule of a particular base sequence of base-paired double stranded nucleic acid. The solid lines represent interactions of abundant versatility. The very thick line emphasizes that for any sequence of the usual monomers (base sequence) there is always a complementary base sequence. The diagram does not deal with relatively unspecific interactions, such as the interaction between a particular protein and a DNA backbone independent of the latter's base sequence. The Unpairing Postulate states that the interactions used for control in higher organisms will mainly be chosen from those shown by solid lines in the figure. This implies that double helical DNA will usually have to be unwound at the recognition sites.

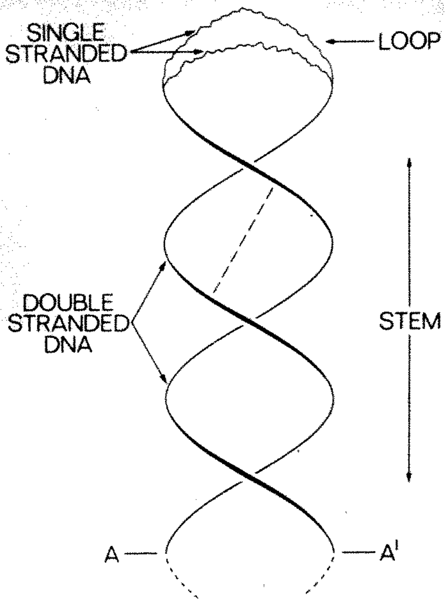

Fig. 3 An example of a possible structural motif within the globular DNA: a twisted hairpin constructed from part of a single length of double stranded DNA. The loop itself has become unpaired due to the untwisting effect produced by the stem. The DNA in the stem remains double stranded and forms a double helical double helix, stabilized by chromosomal proteins, probably mainly by histones. The figure is highly schematic and the details should not be taken too literally. For example, one type of histone (either as a monomer or a dimer) may bridge two adjacent helices in the sort of way shown by the dashed line. Another type of histone may do the same by lying horizontally, thus bridging strands on opposite sides of the axis of the structure. The loops themselves may or may not be stabilized in special configurations by chromosomal proteins or by folding back on themselves. Since the histones interact mainly with the backbone[10] of the DNA, with little respect for base sequence, the actual base sequence of the lengths of DNA in the stem is not important, at least to a first approximation. The loops are postulated to be the sites of the actual control elements. Any particular loop may have an unwinding sequence (to help localize the unwinding—possibly a sequence of A's on one strand), a promoter sequence for the RNA polymerase, or an operator sequence (whether for positive or negative control is left open) or, more likely, some combination of these sequences. The base sequences for the first two functions may be much the same in very many different loops. The operator sequences may or may not be repeated in various other loops, but in general such sequences are likely to be repeated rather less often than the other two types postulated. An occasional loop may contain an initiator sequence for DNA replication. Since the normal DNA double helix is right handed, the superhelix is more likely to be left handed (as shown in the figure) for mechanical reasons. I thank Drs Graeme Mitchison and David Baillie for instructing me on this point. Strictly speaking, either hand is possible for the superhelix if the histones can distort the basic twist of the DNA double helix in the appropriate way. If the second type of histone postulated above interacts with its neighbours (above and below, near the axis of the structure), this interaction could itself impose one particular hand of twist, since protein molecules are intrinsically handed. The structure shown is only one of a family of similar structures. The simple helical double helix is the first member of the family. Another example could be constructed by intertwining a pair of hairpins (of double helical DNA) to form a stem having a quadruply helical double helical structure, with four single stranded stretches in the loop region. Whether the single strands within a loop region can interact, by complementary base pairing, with similar stretches in other loops in the same "band" of a single chromatid (or also, in the second structure mentioned, within the same loop region) is an open question. I expect this to happen in the highly repetitive "satellite" sequences[13] found in the heterochromatin near the centromeres[14,15]. In the euchromatin the answer must, in part, depend on the relative location of different hairpins within the "band" of one chromatid. This is not easy to decide, although various attractive models are possible. (For example, a double-headed structure might be formed, roughly described by the operation of a dyad axis along the line AA′ in the figure.) Be that as it may, the single stranded regions are postulated to mediate the highly specific lining up of the bands of the polytene chromosome[7] by forming complementary base-pairs between adjacent "chromatids" in the same band. A similar interaction may perhaps take place in meiosis.

some tens of thousands for man. It is not, however, completely excluded that, in special cases, multiple coding sequences may be hidden within some of the globular bands, in which case the numbers could be higher. The amount of these special bands, if they exist, might differ markedly in different kinds of higher organisms.

The model, which is logically coherent, appears to me to be compatible with a very large amount of experimental data obtained using very different techniques. These include rough estimates from genetic data[16] of the number of "genes" in *Drosophila* and man, the correlation between the number of bands plus-interbands and genetic complementation groups[17], the specific pairing between the bands of the giant polytene chromosomes[7] shown by the study of inversions and so on, the nature[13-15] and general effects of the heterochromatin[18], the large amount of data on nucleic acid hybridization[1,19] and the formation of circles by the technique of Thomas and his colleagues[20].

It can also be accommodated to the data on the "puffing" of polytene chromosomes[4], the general nature of the heterogeneous rapidly turning over nuclear RNA[21-24] and the apparent absence of polycistronic messengers in higher organisms. It is not incompatible with the very scanty X-ray studies of chromatin[12,25] and the electron microscope pictures and measurements[11].

Although the model is speculative and not fully detailed, and raises at least as many questions as it attempts to answer, I hope it may serve as a focus for discussion and for the design of experiments.

In addition to thanking many colleagues for their patience in explaining their results and for discussing these problems with me, especially Sydney Brenner, Leslie Orgel, Peter Walker (see his remarks reported in ref. 26), Gordy Tomkins and David Baillie, I thank especially the organizers of the specialists' meeting in May of this year at Port Cros[26] for inviting me to attend.

Note added in proof. On the amount of informational DNA in higher organisms see T. Ohta and M. Kimura, *Nature*, **233**, 118 (1971).

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LETTERS TO NATURE

PHYSICAL SCIENCES

Charged Particle Track Registration in Amber

Ionizing charged particles can leave damage trails in certain dielectric solids which, in suitable conditions, can be chemically etched into visible, usually cone-shaped, tracks[1-3]. Such tracks have been widely studied in minerals, glasses, and synthetic polymers[4], but damage tracks in natural resin solids such as amber have not previously been studied.

Some amber deposits in England[5] are of Carboniferous age (345 to 280 m.y.) whereas the age of Baltic deposits[5,6] is thought to be Eocene–Oligocene (about 40 m.y.). Amber samples may, therefore, have recorded certain rare cosmic ray events such as the passage of magnetic monopoles. Furthermore, if ^{238}U spontaneous fission fragment trails are preserved in the amber for a sufficiently long time, then in principle the track dating technique[4,7-9] should be applicable to the dating of amber deposits. In this communication we describe the etching of fission fragment tracks in amber and present data on the ionization damage threshold for track registration, on the annealing of formed tracks, and on the abundance of ^{238}U.

A quite satisfactory etching solution for amber was found to be 30 g of $K_2Cr_2O_7$ in 150 cm^3 of H_2SO_4 (33%). Fission fragment tracks from ^{252}Cf could be observed after etching for 1 h at a temperature of 75° C. At lower temperatures, the etching rate was much lower but the ratio of etching rate, V_T, along the particle track to general surface etching rate, V_g, increased and the half-cone angle at the tip of the track, given by arcsin (V_g/V_T) decreased, a most desirable trend because both particle track visibility and the maximum incidence angle relative to the material surface for track registration are thus improved. At 28° C, the cone angle was found to be $38° \pm 5°$, at 40° C it was $42° \pm 5°$, at 78° C it was $60° \pm 8°$, and at 90° C no tracks were observed. Typical ^{252}Cf fission fragment tracks after etching at 40° C are shown in Fig. 1. This etching temperature was used throughout the work to be described.

All synthetic plastics studied so far have significantly lower ionization damage thresholds for particle track registration than crystalline solids, minerals, or glasses[10]. The very complicated differential etching process as well as the complex details of damage formation have precluded the formulation of a quantitative theory of track registration. Qualitatively, it has been thought that the ionization damage leading to track formation in plastics is lower because polymer chains are more readily broken in a plastic than atomic displacements are produced in a crystal or glass. These qualitative features are represented in the so-called "ion-spike" model of track formation[10]. Amber, being a resin material, would be expected to have a lower threshold than minerals or glasses but we find that it has a very high threshold, larger even than those of the meteoritic minerals which have the highest of the previously measured thresholds.

Table 1 Track Formation of Amber relative to Mica and Diopside

Absorber thickness (mg cm^{-2})	Track density relative to that of mica at zero absorber thickness			
	Mica	Amber	Diopside[3,11]	Mica[3,11]
0.88	1	1		
1.1	1	1/2		
1.32	1	1/10		
1.476			> 1/2	
1.54		0		
1.607			0	> 1/2
1.76	1/2			
1.914				0
1.98	1/10			
2.2	0			

Table 1 shows the track formation properties of amber relative to mica (muscovite) as studied using slowed ^{252}Cf fission fragments. Various thicknesses of polycarbonate sheets were placed between the fission source and the amber and mica samples, which were then irradiated for identical times. The agreement between the earlier results for mica and diopside[3,11] and the results of our work is satisfactory in view of the 10% uncertainty in absorber thickness. There were no tracks formed by ion beams of ^{20}Ne at 10 MeV a.m.u.$^{-1}$ and ^{37}Cl at 2 MeV a.m.u.$^{-1}$ at normal incidence.

Track fading can occur due to thermal annealing of the damage regions[4,7-9]. Phenomenologically, the fading can be

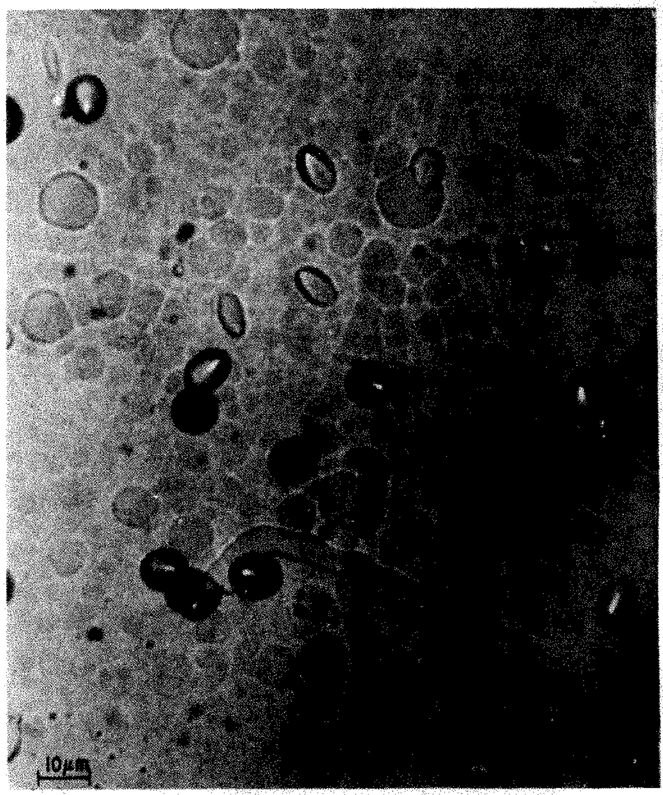

Fig. 1 ^{252}Cf fission fragment tracks in amber.

described in the form

$$\tau = A \exp (E/kT) \qquad (1)$$

where τ is time required for a certain degree of track fading. The activation energy E and the factor A can be determined by several measurements of track fading at different temperatures. It is then assumed that this relationship can be extrapolated to geological times. In those instances where verification was possible, this extrapolation has proved to be valid[4].

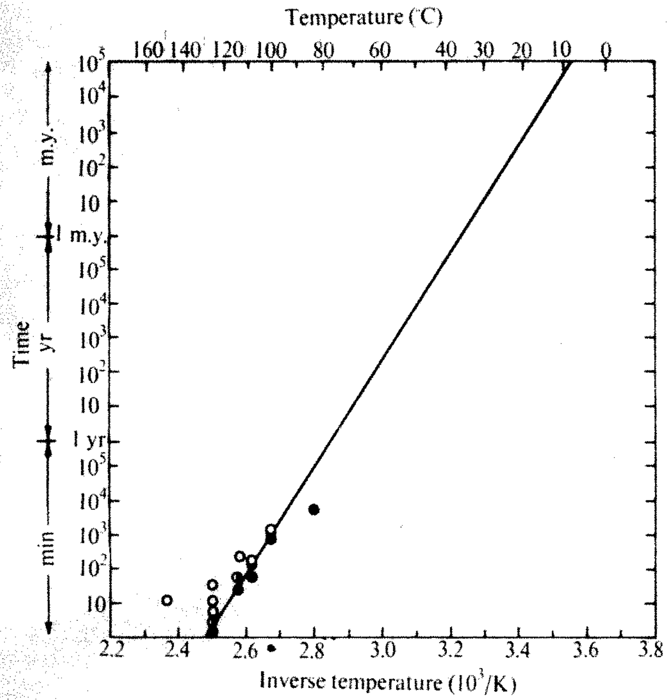

Fig. 2 Fission fragment track fading results for amber. —, Approximate onset of fading; ●, tracks not faded; ◑, partial track fading; ○, total track fading.

Annealing effects for amber in accordance with equation (1) are shown in Fig. 2; ^{252}Cf fission fragments were again used. An activation energy of 3 eV can be deduced from the slope of the data on complete removal of tracks. An exposure of 1 h at 115° C was sufficient to remove fission fragment tracks completely. We conclude that, at a mean temperature of 30° C, fission tracks from ^{238}U decay are retained for approximately 10 m.y., and at 20° C for 450 m.y. Given a sufficient uranium abundance, it would seem that amber would be suited to the particle track technique of dating[4,7-9]. The deposition of amber in relatively shallow strata or marine basins would not heat the material above 30° C for long periods. Therefore, from Fig. 2, we may conclude that the tracks from ^{238}U fission would remain from the fossilization period to the present time. Because age determination from stratigraphic and palaeontological data is relatively poor and because no other radiometric dating on amber has been successful[5], the track technique may potentially provide unique information on amber age.

It is unfortunate that the great age of amber is not coupled with a lower track registration threshold. Mica (muscovite) and obsidian have been scanned for magnetic monopole tracks and these studies have set rather stringent limits on the flux of magnetic monopoles of various masses and magnetic charge numbers greater than 2 (ref. 12). The high threshold of amber precludes its use for registering monopoles of charge 1 and charge 2, and allows it to be used only in a monopole charge-mass region which has already been well explored[13].

Uranium abundance in amber has not been reported previously. We have determined the ^{238}U content in our amber samples (collected near Gdansk, Poland) by inducing ^{235}U fission and then observing the fragment tracks[14]. Because of heating effects in reactor neutron irradiations we chose to count the induced ^{235}U fission events not in the amber but in mica placed immediately around the amber sample*. The same neutron dose irradiated the mica–amber–mica sandwiches as well as two mica–glass–mica dosimetry samples. From the known U content of the glass we have deduced the ^{238}U abundance in seven different amber pieces. The average ^{238}U content of samples 1, 2, 3, and 5 is approximately 0.001 to 0.004 p.p.m. by weight. Samples 4 and 6 contain 0.5 to 0.7 p.p.m. and sample 7 has 0.03 to 0.08 p.p.m. In sample 4, large quantities of impurities were present as visible inclusions dispersed throughout the amber. On the other hand, sample 6 was free of particles but contained densely dispersed bubbles. These last two samples could not be scanned very effectively because of the surface imperfections due to inclusions and bubbles.

No natural fission tracks were observed for an effective scan area of 0.3 cm^2 on samples 4 and 6. Thus the oldest track storage age consistent with both the annealing curve and the measured ^{238}U abundance is about 350,000 yr for a 90% confidence level (for Poisson statistics there is a 10% probability for zero events if the mean number of events is 2.3). If the samples are older, as indeed it is believed that they might be, then they evidently remained at temperatures above 35° C for most of the time. A very careful scan of sample 2 over an area of 3 cm^2 revealed no tracks. We estimate the maximum retention age, with a uranium content of two parts per billion, to be 8 m.y. (90% confidence level).

Although we were careful not to expose the amber specimens to track annealing temperatures, we have no knowledge of the thermal history of our amber samples. If we assume that no track annealing has occurred recently, there are several other possible explanations for the absence of natural fission tracks. The amber samples may be much younger than the country rock in the Baltic region and the mean temperatures of samples 4, 6, and 2 may have been about 37° C, 37° C, and 30° C respectively. It is also possible that the extrapolation of the annealing curve to geological times is not valid for amber.

Although amber is not suitable for observing magnetic monopoles of charge 1, the high threshold of amber indicates that it may well be a useful solid track detector in studies that require rejection of events caused by lightly ionizing fission fragments or similar particles. Whether the absence of natural fission tracks in amber is peculiar to our samples or whether it it is a result to be generally expected for amber is a question that needs further examination.

The amber samples were kindly provided by Professor H. Faul, University of Pennsylvania.

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Time Dependence of Variances of Sonic Boom Waveform

In a series of experiments[1] performed in November and December 1966, at Edwards Air Force Base, California, sonic boom pressure signatures were recorded at forty-two ground level microphones, equally spaced in an 8,000 foot linear array, during level overflights of F-104 fighter aircraft at flight Mach numbers of approximately 1.3 and at an altitude of approximately 30,000 feet. The array was almost directly beneath the flight track. The variations in the signatures recorded by different microphones during the same overflight are believed to be caused primarily by atmospheric turbulence. This communication reports an analysis of the variations in these data and considers the extent to which the analysis substantiates a recent theory[2].

Crow's theoretical model consists of a linearized first order transient scattering theory for an initially plane wave step of overpressure incident on the Earth's turbulent boundary layer from above. The turbulence is considered isotropic and quasi-homogeneous. Eddies in the Kolmogorov inertial subrange (where turbulent structure functions vary with separation distance r as $r^{2/3}$) are considered to be the chief source of the waveform variations for times somewhat later than the principal shock arrival. An important result of the analysis is the relation

$$\langle \psi^2(t) \rangle = (t/t_c)^{-7/6} \tag{1}$$

for the ensemble average of the square of the ratio $(p^S)/\Delta p_0$. Here (p^S) is the scattered wave minus a phase shift term (formally appearing as a multiple of a Dirac delta function), which represents the increment that may be added to the incident wave to account (to first order) for the change in time of onset caused by transit speed fluctuations. The quantity Δp_0 is the overpressure of the incident step pulse. The parameter t_c is a somewhat complicated function of (height dependent) parameters characterizing the atmosphere's state of turbulence in the inertial subrange.

Although a previous experimental check on Crow's theoretical relation has been made by Bauer and Bagley[3], using waveforms recorded on the wall of an extended ballistic range, with boundary layer turbulence created by a jet adjacent to the wall, the results are somewhat ambiguous because of the dissimilarity between the laboratory turbulence and that of the atmosphere. Our analysis is, however, based on actual field data.

We consider the set of forty-two microphone pressure signatures recorded during a given overflight to constitute a representative sample of what might be obtained during an ensemble of similar experiments. The choice of time origin for any given sample is taken as that time at which the overpressure first reaches 1/3 its peak value (see inset in Fig. 1). This choice is based on the premise that Crow's equation (1) is intended to apply when t is relative to time of actual wave onset. Onset is difficult to define unambiguously for waveforms with finite rise times, so some specific definition of onset must be made. It would appear, however, that any results comparable to those reported here are relatively insensitive to this definition.

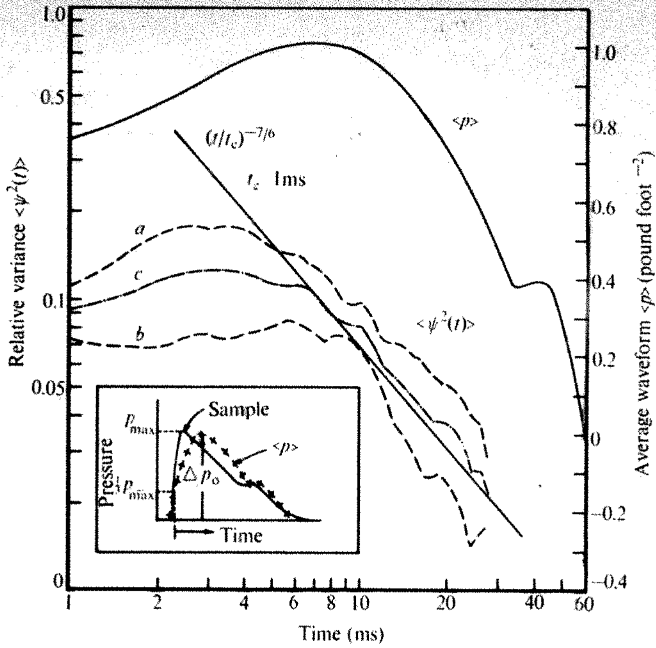

Fig. 1 Time variation of relative variance $\langle\psi^2(t)\rangle$ and of mean overpressure $\langle p\rangle$ of sonic boom waveforms. The three plots of $\langle\psi^2(t)\rangle$ correspond to computations based on data corresponding to (*a*) flight 16, (*b*) flight 17 and (*c*) combined data for both flights. The single graph of $\langle p\rangle$ corresponds to the combined set of data. The inset indicates the choice of time origin for sample waveforms, as well as the definition of maximum overpressure Δp_0 of the mean waveform. The negative phase of the waveform is not sketched.

The mean waveform $\langle p\rangle$ and variance $\langle\{p-\langle p\rangle\}^2\rangle$ are estimated from a computation of the numerical averages of $p_i(t)$ and $\{p_i(t)-p_{ave}(t)\}^2$ for the set of sample signatures. The relative variance $\langle\psi^2(t)\rangle$ is defined as

$$\langle\psi^2(t)\rangle = \langle\{p-\langle p\rangle\}^2\rangle/(\Delta p_0)^2 \tag{2}$$

where Δp_0 is the peak overpressure of the average waveform, is estimated similarly. Although sonic boom signatures are shaped somewhat like the letter N, a correspondence between this quantity and the $\langle\psi^2(t)\rangle$ in Crow's theory is expected to hold for times at which the variations are approximately equivalent to those induced by the propagation of a step pulse.

In Fig. 1, the derived estimates of $\langle p\rangle$ and $\langle\psi^2(t)\rangle$ are plotted for the set of sample signatures corresponding to flight 16, flight 17 and flights 16 and 17 combined. These flights were at 2145 GMT on November 20, 1966, and were spaced approximately 0.5 min apart. As it seemed doubtful whether the parameters characterizing the statistics of the atmosphere's state of turbulence would change appreciably during such a short time, the third computation treated the two sets of data as belonging to the same ensemble. Because any estimate of a variance from a limited number of samples is expected to improve with the number of samples (the expected error decreases as $1/\sqrt{N}$ for a Gaussian distribution) the estimate based on the combined data is considered to be the more accurate. The discrepancy between the three plots should give an indication of the possible range of error in our estimates. (The plot of $\langle\psi^2(t)\rangle$ against time is full log.) Thus during any range of time for which Crow's theoretical relation, equation (1), holds, the plot should approximate a straight line with slope $-7/6$. This seems to be very nearly the case for all three variance curves for times between about 7 and 27 ms. The start of this $-7/6$ regime appears to coincide with the time at which the average waveforms attain their maximum. The upper time limit would seem to correspond roughly to the time at which the second shock begins to arrive. The estimated corresponding value of t_c from the combined data for this particular time, place, and flight profile is very nearly 1 ms with an estimated error of ±0.2 ms.

We believe that these results provide substantial support for Crow's theory, provided that the range of *t* in equation (1) is suitably restricted. The fact that the theory would appear inadequate to account for the variations in the first few ms is not surprising because of the nature of the approximations made in the course of Crow's derivation.

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Experimental Demonstration that the Couple on a Bar Magnet depends on H, not B

IN the macroscopic theory of electromagnetism there are several systems of equations that are compatible with SI units[1,2]. Among these are two important ones in current use which differ in their treatment of certain magnetic quantities. In one of these, introduced by Giorgi[3], but now named after Kennelly, the field acting on a magnetic pole is considered to be the **H**-field, giving the couple **T** acting on a long thin magnet of moment **j** immersed in a linear magnetic medium as

$$\mathbf{T}=\mathbf{j}\times\mathbf{H} \quad \text{(Kennelly)} \tag{1}$$

The degree of magnetization of a material is denoted in this system by

$$\mathbf{J}=\mathbf{B}-\mu_0\mathbf{H} \quad \text{(Kennelly)} \tag{2}$$

In the other system, introduced by Sommerfeld[4,5] (but differing from the one attributed to him by the Coulomb's Law Committee[18]), emphasis is placed on the **B**-field and the equation for the couple on a long thin magnet of moment **m** is

$$\mathbf{T}=\mathbf{m}\times\mathbf{B} \quad \text{(Sommerfeld)} \tag{3}$$

In this system the degree of magnetization of a material is represented by the quantity

$$\mathbf{M}=\mathbf{B}/\mu_0-\mathbf{H} \quad \text{(Sommerfeld)} \tag{4}$$

There is no difference between the Kennelly and Sommerfeld systems as far as the measures of **B** and **H** are concerned.

The relative merits of these systems of equations are a matter of current controversy and the use, without explicit specification, of alternatives within the commonly adopted framework of SI units is a source of much confusion. The International Electrotechnical Commission[6,7] recognizes both systems and specifies names, symbols and definitions for all four quantities **j**, **J**, **m** and **M**; the definitions of **j** and **m** are based on equations (1) and (3) respectively. The International Union of Pure and Applied Physics[8,9] and the Royal Society[10] have, however, omitted the Kennelly moment (**j**) from their lists of recommended symbols although they retain the magnetic polarization **J**. The Institution of Electrical Engineers gives no symbol for any of these quantities in its list[11], but it quotes the Bohr magneton in Kennelly units. SI itself is a system of units[12] and, although it specifies the appropriate unit for each physical quantity once that quantity is defined, it makes no statement about the merits of different systems of equations[13]. It is systems of equations that are being considered in this communication.

The choice between the Kennelly and Sommerfeld systems of equations is often said to be quite arbitrary (ref. 14, for example). This is not the case, as can be seen from the following argument. In any reasonable system one expects that "the whole is the sum of its parts" and, in this context, this implies that the moment of a magnet should be given by the integral of its magnetic polarization (or magnetization) over the volume of the magnet itself. This is expressed by the equations

$$\mathbf{j}=\int\mathbf{J}\,\mathrm{d}V \quad \text{(Kennelly)} \tag{5}$$

$$\mathbf{m}=\int\mathbf{M}\,\mathrm{d}V \quad \text{(Sommerfeld)} \tag{6}$$

Comparison of equations (2) and (4) shows that **J** and **M** at any point in a material differ only by the force constant μ_0 and equations (5) and (6) therefore imply that for any magnet

$$\mathbf{j}=\mu_0\mathbf{m} \tag{7}$$

Now a long thin magnet immersed in a linear permeable fluid medium and subjected to an external magnetic field $\mathbf{B}=\mu_r\mu_0\mathbf{H}$ experiences an observable couple given by equations (1) and (3). Comparison of these equations shows that

$$\mathbf{j}=\mu_r\mu_0\mathbf{m} \tag{8}$$

which is contrary to equation (7). The equations of the set (1) to (6) are therefore not mutually compatible. The error may be located in various places depending on one's point of view. If we take equations (2), (4), (5) and (6) as definitions of **J**, **M**, **j** and **m**, then equations (1) and (3) predict different values for the couple on a long thin magnet immersed in a permeable medium. One of these two equations must therefore be wrong. If, however, equations (1) and (3) are treated as definitions of **j** and **m**, we find that, even for a "hard" magnet, **j** and **m** cannot both be independent of the surrounding medium and equations (2), (4), (5) and (6) cannot all be true.

This problem is important, not because magnets immersed in media are of practical significance, but because it impinges on fundamental questions about the formulation of the macroscopic theory of electromagnetism. The topic was first raised many years ago. Maxwell followed what is essentially the Kennelly approach, but Clausius[15] asserted that he was wrong. A discussion ensued in which Thomson[16] recognized the importance of the permeability of the medium and pointed out that the matter could be subjected to experimental test. An experiment was performed by Sargant[17] but his account is brief and the outcome unclear. More recently Sommerfeld[4] has asserted that Maxwell was in error in claiming that the force on a magnetic pole depends on **H**, and in his book[5] he clearly establishes his system as factually different from the Maxwell–Kennelly approach.

Discussion still continues entirely on the basis of theoretical argument, but we have now subjected these arguments to experimental test by determining the couple on a long thin magnet immersed in a magnetic medium. The magnet was hard in the normally accepted sense that the internal state of polarization (**J** or **M** defined from (2) or (4)) was independent of the medium. If this is taken to imply that the moment of the magnet does not change on immersion in the medium, the experiment provides a test of equations (1) and (3) and can thus distinguish between the correctness of the Sommerfeld and Kennelly systems.

Fluid media are only weakly magnetic and it would be very difficult to make measurements of couples and fields with sufficient accuracy to test equations (1) and (3) directly. We therefore used a null method in which the couple on the magnet was balanced by the couple on a current-carrying coil placed in the same field; the current *I* for which the couple on the coil equalled that on the magnet was measured in two media of differing permeability. The couple on a current loop, completely immersed so that the medium passes through the loop, is proportional to *IB*—a fact that is not in dispute. Thus if the moment of the magnet is invariant and the Sommerfeld equation (3) is correct, the current *I* at balance will be the same for both media, whereas if the Kennelly equation (1) is correct the currents for the two media will differ by a factor equal to the ratio of the permeabilities. In this method the magnitude of the applied field and the effect of changing the

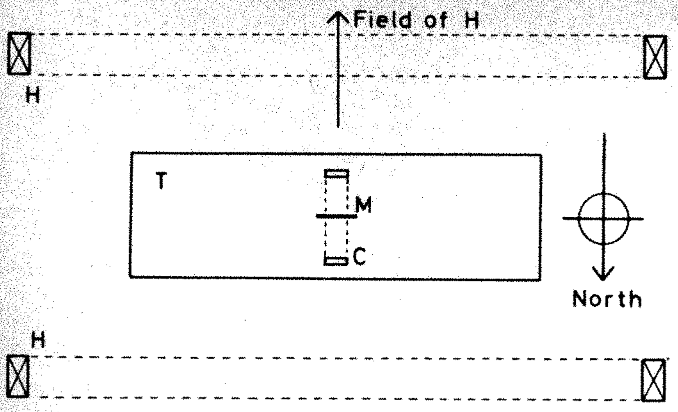

Fig. 1 Horizontal section through apparatus (approximately to scale).

medium on the magnitude of this field are unimportant. What matters is that the change of medium changes the ratio of $\boldsymbol{B}$ to H in the region of the magnet/coil assembly.

A horizontal section through the apparatus is shown in Fig. 1. The coil C had a diameter of 42 mm and was wound with 400 turns; it was suspended on a vertical phosphor-bronze torsion suspension through which its current was supplied. The bar magnet M was of length $l=20$ mm and of square cross-section with side $a=1.55$ mm; it was attached rigidly at the centre of C and its magnetic axis was adjusted in a preliminary experiment to be parallel to the magnetic axis of C to within about 0.002 radian. This assembly was situated at the centre of a 'Perspex' tank measuring $20\times20\times6$ cm which could be filled either with water or with a 4 M solution of $MnCl_2$. An external field of approximately 180 A m^{-1} could be applied from a pair of Helmholtz coils H (diameter 31 cm) lying outside the tank; this field was parallel to the horizontal component of the Earth's field and perpendicular to the large face of the tank. In all measurements the axis of the suspended coil/magnet assembly was perpendicular to the external field as shown in Fig. 1.

With water ($\mu_r=1.00000$) in the tank, a determination was made of the current in C such that no motion of the suspended system occurred when the field of the Helmholtz coils was switched on and off. This current was approximately 57 mA and was determined to an accuracy of about 1.5 µA. The experiment was then repeated with the $MnCl_2$ solution in the tank. The magnetization of a magnet varies with temperature and the temperature of the liquid was therefore measured at a point close to the magnet. The currents at balance were determined at three temperatures in each medium; the results are plotted in Fig. 2 and parallel lines have been drawn through the two sets of points. At a given temperature the balancing current is different for the solution and for water, and their ratio was found to be 1.00065 ± 0.00005. The relative permeability of the liquid measured by Quincke's method was 1.00067 ± 0.00002.

The magnet was a bar of Magloy 2 (supplied by the Plessey Company Ltd), magnetized in an electromagnet and stabilized by applying a reverse field to reduce its magnetic polarization at zero field by about 10%. After removal from the electromagnet, its moment (in Kennelly units) was 4.0×10^{-8} Wb m; in this state the polarization was non-uniform, with an average value of about 90% of its uniform value before removal from the electromagnet. It is necessary to establish that the magnet was "hard" in the sense that changes in its polarization on immersion in the $MnCl_2$ solution could be neglected. These changes occur because the surrounding medium modifies the demagnetizing field $\mathbf{H}$ at each point in the magnet, and so produces changes in the value of $\mathbf{J}$ at each point. As the magnet had been cycled several times between air and the $MnCl_2$ solution before the start of the experiment itself, further changes of this type corresponded to moving the working points of all portions of the magnet along the appropriate recoil lines in the J–H diagram. Considering axial components, the change in J for a change δH in H will then be $(\mu_{rec}-1)\mu_0\delta H$, where μ_{rec} is the recoil permeability, given by the manufacturers as approximately 3.8. In changing the surrounding medium from a medium of relative permeability 1 to one of slightly greater relative permeability μ_r, the maximum fractional change that can be produced in H at a point inside the magnet is $-(\mu_r-1)$. The maximum fractional change in the magnetic moment of the magnet is therefore

$$-(\mu_r-1)(\mu_{rec}-1)\mu_0\frac{\int H\,dV}{\int J\,dV}$$

where the integrals are evaluated over the volume of the magnet; equation (5) has been assumed to be valid. An upper limit to $\int H\,dV$ can be estimated by calculating the field H at points on the axis of a uniformly polarized bar and imposing the condition that the value of H near the ends cannot exceed the coercive field of the material (6.2×10^4 A m^{-1}). Such calculations show that the fractional increase in the magnetic moment of the magnet on immersing it in the $MnCl_2$ solution is not more than $0.07\,(\mu_r-1)$. The change in the current in the suspended coil produces a change in its field at the magnet but the ensuing fractional change in moment is only $0.003\,(\mu_r-1)$. Within the limits of the error of this experiment the magnet may therefore be taken to be hard.

It was implicitly assumed in the description of the underlying theory of the experiment that the magnet and the coil were situated in a uniform field so that the same field acted on them. In practice the applied field was not perfectly uniform so that, even *in vacuo*, the effective field acting on the magnet differed from that acting on the coil. We are concerned only with the change in the balancing current I produced by the presence of the medium and the important matter is therefore the way in which the small field produced by the polarization of the medium modified the degree of inhomogeneity of the original Helmholtz field. The size of this effect was computed, using experimentally determined values for the profile of the Helmholtz field and taking into account the finite size of the tank of liquid used, but errors from this source were found to be negligible.

The experiment shows that the ratio of the balancing current when the system is immersed in the $MnCl_2$ solution to that when immersed in water is, within experimental error, equal to the reciprocal of the relative permeability of the solution. The ratio of the balancing currents is definitely not unity. If we take the moment of the magnet to be independent of the surrounding medium, this result is consistent with the Kennelly

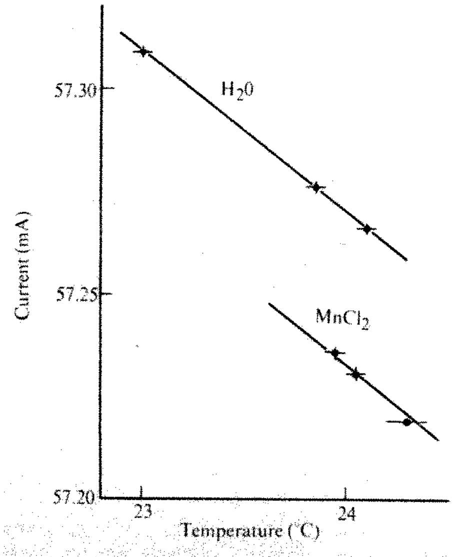

Fig. 2 Balancing current in coil as a function of temperature.

equation (1) and not with the Sommerfeld equation (3). Allowance for any change in the moment of the magnet due to insufficient hardness could not reverse this conclusion because the effect does not have the required sign. We therefore conclude that the couple on a long thin hard magnet which has a constant magnetic moment **j** is given by the Kennelly equation

$$\mathbf{T} = \mathbf{j} \times \mathbf{H}$$

This equation applies to a long thin magnet, which is the system that comes most naturally to mind when thinking of a "dipole". In general, however, the couple on a magnet in a medium will depend on its shape. For a disk-like magnet magnetized perpendicular to its plane with a magnetic moment **j** (defined from (5)), the couple in the Kennelly system is given by

$$\mathbf{T} = \mathbf{j} \times \mathbf{B}/\mu_0 \qquad (9)$$

The corresponding equations for electrically polarized matter are:

$$\text{needle shape: } \mathbf{T} = \mathbf{p} \times \mathbf{E} \qquad (10)$$

$$\text{disk shape: } \mathbf{T} = \mathbf{p} \times \mathbf{D}/\varepsilon_0 \qquad (11)$$

It is not possible simply to say that the experiment shows that equation (1) is correct whereas equation (3) is false for, as has already been indicated, these equations can be treated as definitions of the moments **j** and **m**. If this is done, the experiment shows that **j** is invariant on immersion in a magnetic medium, whereas **m** is not. This is contrary to the position adopted by Sommerfeld who states that his measure of dipole moment is conserved whereas the Kennelly measure is variable (ref. 5, pages 41 and 87—the statement is actually formulated in terms of poles). Any attempt to formulate a system of electromagnetism based on equations (3) and (4) necessarily involves abandoning equation (6). This is not generally recognized by users of the Sommerfeld system; the *International Electrotechnical Vocabulary*[6], for example, defines the "moment magnétique ampèrien d'un aimant" by equation (3) and adds a statement which appears equivalent to (6); but it is hard to believe that they are advocating the abandonment of equation (4).

We are led to the conclusion that any system in which the couple on a magnet is written as $\mathbf{m} \times \mathbf{B}$ is misleading, and the full system of electromagnetism as formulated by Sommerfeld[5] is in error. Sommerfeld's system has, however, sometimes been incorrectly stated and, although Sommerfeld's equations are correctly stated in the review by Smith[14], the report of the Coulomb's Law Committee[18] has caused much confusion by attributing to Sommerfeld a system of equations which is not his[1,2]. In particular, equation (3) is replaced by $\mathbf{T} = \mu_0 \mathbf{m} \times \mathbf{H}$ or its equivalent. This removes the factual error but makes the system non-Sommerfeld in character even though the units of magnetic moment are the same as those appropriate to Sommerfeld's system. Once it is recognized that systems which use equation (3) are unacceptable, there remain several possible systems which differ from the Kennelly system only in matters of convention regarding the places at which μ_0 is introduced. The system developed by the Coulomb's Law Committee and wrongly attributed to Sommerfeld is one of these alternatives. The problem is more complex than a choice between "Kennelly units" and "Sommerfeld units" for the mere specification of units leaves ambiguity about the equations and quantities intended.

We do not intend to draw deep theoretical conclusions nor to discuss the relative merits of the alternative systems of equations that are physically correct. One immediate consequence of the experimental result is, however, evident when equation (1) is compared with equation (10) and equation (9) with equation (11). If there is a dualism between electric quantities and magnetic quantities in the macroscopic theory of electromagnetism, then the magnetic field corresponding to the **E**-field is the **H**-field and not the **B**-field. It can be shown that there is such a dualism; it is seen clearly in the tensor formulation of the special theory of relativity.

It is, of course, often convenient to refer to the magnetic moment of a current loop. If this is defined by $\mathbf{m} = I\mathbf{A}$ or $\mathbf{j} = \mu_0 I\mathbf{A}$ the appropriate equations for the couple on such a loop are equations (3) and (9) respectively. A coil which is permeated by the ambient medium responds to the **B**-field whatever its shape but a coil with an evacuated core behaves like a magnet of the same shape; this is a consequence of the Ampèrian theory of the magnet.

The conclusions of this paper can be reached from the basic concepts of electromagnetism and, indeed, many authors have done this. Nevertheless the importance of the **B**-field in problems of current electricity has led many others to incorrect conclusions. The subject is of immediate importance because of the danger that decisions about standardization of systems may be taken in the belief that only matters of convention need be considered. We have set out to demonstrate that matters of physical fact are involved, and we hope that the introduction of an experimental result into the discussion will be a helpful clarification.

The general secretary of the International Electrotechnical Commission has asked us to state that the chairman of the IEC Technical Committee No. 1, Terminology, which is responsible for the *International Electrotechnical Vocabulary*, is aware of the problem and that the points raised in this communication will be considered in the work of revision which is now taking place.

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Algorithm for the Production of Contour Maps from Linearized Data

COLE has proposed an algorithm which produces a generalized surface for contouring scattered data[1]. The algorithm works well when the data points are randomly distributed but improbable results have been obtained when the data points are distributed along lines. There are two reasons for this: one is the extrapolations which occur into regions without data and the other is the generation of unlikely gradients

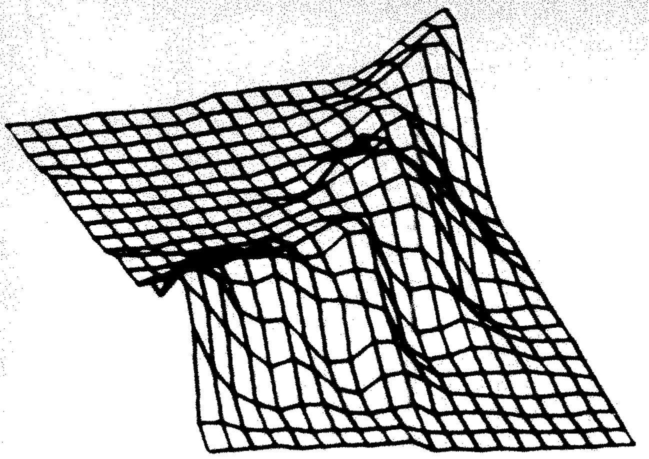

Fig. 1 A perspective grid derived from a matrix of values computed from linearized measurements.

across the lines. Measurements of many geophysical properties, made by moving vehicles, ships and so on, are often distributed along lines which are not necessarily straight. They may cross one another but the distance between adjacent measurements on the lines is usually much less than the distance between the lines. Such a distribution of measurement points may be found in other situations where the two dimensions are not spatial.

By Cole's method, the generalized surface is actually a matrix of Z values and the initial values of the matrix elements are derived from a global least squares fit of a second-order two-dimensional polynomial function. This global surface is then modified by a local least squares quadratic fit involving the 3 by 3 matrix around each data point. The modified matrix is then smoothed by means of an algorithm which removes discontinuities of gradient between the global and local surface but does not affect quadratic surfaces. The algorithm is made iterative by using the matrix obtained as the new global surface for a repeat of the process. The effect of this is the production of a smooth surface which passes through the data points. In areas where data are absent, the algorithm tends to extrapolate first and second derivatives. In practice this may be undesirable. Imagine a string of data points passing over a hill in the measured property. If the path deviates slightly from a straight line as it crosses the hill, this would be interpreted as a steep slope perpendicular to the track. But this would not be the subjective evaluation of the data, because such steep slopes are not found along the path of measurement. When the source data are linearized, more information is available about the statistical nature of the surface. I have therefore modified Cole's algorithm to improve these two aspects—the extrapolation of first and second derivatives, and the use of the statistical information. It is necessary to specialize somewhat because I propose that on a large scale neither the first nor second derivatives of the measured property can be extrapolated indefinitely. Instead, in any areas without data, we may expect a horizontal plane: this is true for many geophysical measurements but may not be valid for other types of property. Bearing this in mind, each element of the initial matrix of Cole is set equal to the value of the nearest data point. Then a single data point yields a single-valued plane, and at points away from the data the resultant surface tends to the value of the nearest data point. In this way improbable cross track gradients are not generated because initially the matrix values at either side of the track are equal to the value on the track, although there will in general be discontinuities between tracks. If the property being contoured has known discontinuities within the area of the matrix, in particular if there is a boundary (such as a known coastline) beyond which contours should not be plotted, then any data from beyond the boundary are omitted (the survey is discontinued at the boundary) and, after contouring, the plane surface which will extend beyond the boundary into the area of no data is omitted. The local quadratic least squares fit of Cole has been retained because on a small scale these extrapolations are permitted. The principal change to Cole's algorithm is in the smoothing. The source data are scanned along the survey lines and the root mean square gradient between adjacent data points is determined. We may now assume that the function which has been measured has statistical properties which are isotropic. To be more specific, I assume that the mean square gradient observed along the track is the same as that expected across the track. We may therefore smooth the matrix obtained by an amount which increases rapidly for gradients greater than the r.m.s. gradient determined along the track. The gradient in the vicinity of each matrix point is found, and the Z value changed by an amount $\Delta Z\, a/(1+a)$ in such a way as to reduce the gradient; a is the ratio between the local gradient and the r.m.s. measured gradient. Thus a matrix is produced representing a surface which passes through the data points and has the same statistical properties as the source data. This method is only possible because the data are distributed along lines, and it is not suitable for randomly scattered data. The matrix obtained is then contoured by a standard computer routine to produce a contour map. Alternatively, it is worth considering a perspective grid as shown in Fig. 1.

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Distance between Sets

Distance functions expressing the degree of dissimilarity of sets have found use in physical anthropology[1], psychology[2], numerical taxonomy[3], ecology[3] and elsewhere. During an ecological study by one of us, it was noticed that the similarity coefficient of Jaccard[6], used in ecology, gives rise to a metric function satisfying the triangle inequality. For two non-empty finite sets X, Y, the Jaccard coefficient is the number of elements in the intersection $X \cap Y$ of X and Y. This coefficient

$$r = \frac{|X \cap Y|}{|X \cup Y|}$$

(we use absolute value signs to indicate number of elements) has a heuristic interpretation. It measures the probability that an element of at least one of two sets is an element of both, and thus is a reasonable measure of similarity or "overlap" between the two. The one-complement

$$d(X, Y) = 1 - r(X, Y) \qquad (1)$$

may then be considered a measure of the dissimilarity of the two sets.

To study patterns of similarity or relatedness of sets of data, it is often helpful to represent them abstractly as points in a space, which can be studied by the methods of cluster analysis or ordination. For this, it is an advantage if the measure of dissimilarity has the formal properties of a metric or distance function.

If X, Y and Z are non-empty finite sets, we claim that

$$d(X, Y) + d(Y, Z) \geq d(X, Z) \qquad (2)$$

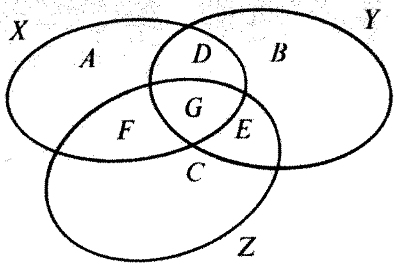

Fig. 1 Representation of sets and subsets.

By the definition of the function d, this reduces to showing that

$$\frac{|X\cap Y|}{|X\cup Y|}+\frac{|Y\cap Z|}{|Y\cup Z|}\leq\frac{|X\cap Z|}{|X\cup Z|}+1 \qquad (3)$$

We break up $X\cup Y\cup Z$ into seven disjoint subjects A to G which we use to transform inequality (3) into a manageable form. Thus

$$X\cup Y\cup Z=(A\cup B\cup C)\cup(D\cup E\cup F)\cup G$$

where

$$A=X-(Y\cup Z),\ B=Y-(X\cup Z),\ C=Z-(X\cup Y),$$
$$D=X-(A\cup Z),\ E=Y-(X\cup B),\ F=Z-(C\cup Y),$$
$$G=X-(D\cup F\cup A)=Y-(D\cup E\cup B)+Z-(E\cup F\cup C)$$

This is best understood from Fig. 1.

If $a, b, c, \ldots$ denote the number of elements in the corresponding sets A, B, C, . . . , the inequality (3) becomes

$$\frac{d+g}{v-c}+\frac{e+g}{v-a}\leq\frac{f+g}{v-b}+1 \qquad (4)$$

where $v=a+b+c+d+e+f+g$, the number of elements of $X\cup Y\cup Z$. Symbolically written, the inequality (4) becomes

$$\frac{d'}{c'}+\frac{e'}{a'}\leq\frac{f'}{b'}+1$$

or

$$a'b'd'+b'c'e'\leq a'c'f'+a'b'c'$$

or

$$(v^2-av-bv+ab)d'+(v^2-bv-cv+bc)$$
$$e'\leq(v^2-av-cv+ac)f'+(v^2-av-bv+ab)c'$$

This inequality is equivalent to $0\leq v^3$

$$\begin{aligned}&+v^2(-a-b-c-d-e+f-g)\\&+v\,[ab+ac+bc+ad+bd+be+ce+2bg-af-cf]\qquad(5)\\&+\{-abc-abd-abg-bce-bcg+acg+acf\}\end{aligned}$$

The second term is equal to $v^2(2f-v)$ so that the sum of the first two terms is $2fv^2$. The inequality now, symbolically, is

$$0\leqslant v(2fv+[\quad])+\{\quad\}$$

Because $v=a+b+c+d+e+f+g$ the two negative terms of $[\quad]$ cancel with terms in $2fv$. And the negative terms of $\{\quad\}$ cancel with terms in $v[\quad]$, namely with terms of the part

$$a(bc+bd+2bg)+b(ce)+c(2bg)+d0+e0+f0+g0$$

of $v[\quad]$. Because all negative terms on the right side of inequality (5) cancel, the inequality is established.

$d(X, Y)$ satisfies the triangle inequality (2) and is also positive definite ($d(X, Y)=0$ if and only if $X=Y$) and symmetric ($d(X, Y)=(d(Y, X))$, so it has the properties of a metric function in a space, the elements of which are finite non-empty sets. The argument presented does not depend essentially on the finiteness of the sets, and the theorem may be generalized by introduction of a suitable measure function for infinite sets.

We have not yet found a simpler or more elegant proof of this theorem based on the theorems of set-algebra. The absence of, or difficulty of finding, such a proof may explain the novelty of the result.

The function d is related to another metric function

$$d'(X,Y)=|X\cup Y-(X\cap Y)|$$

where $X\cup Y-(X\cap Y)$ is the symmetric difference of X, Y in that

$$d=\frac{1}{|X\cup Y|}\,d'$$

for non-empty finite sets X, Y, d', in turn, is a constant times the one-complement of a well-known measure of similarity, the simple matching function

$$r'=\frac{|X\cap Y|+|\overline{X\cup Y}|}{|X\cup Y|}$$

The properties of d and d' are, however, quite different, as one might expect from the probabilistic quality of d in ranging from 0 to 1. The probabilistic and geometric features induced by d are the subjects of further study.

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BIOLOGICAL SCIENCES

Specific RNA Methylase associated with Avian Myeloblastosis Virus

AT least three enzymes of DNA metabolites are found in the RNA tumour virus group—an RNA dependent DNA polymerase[1,2], a DNA dependent DNA polymerase[3] and an endonuclease[4]. We now report that a specific RNA methylase is associated with the avian myeloblastosis virus (AMV) which transfers a methyl group from S-adenosylmethionine to certain guanine bases in RNA to give N^2-methylguanine.

There is linear incorporation of the methyl group of S-adenosylmethionine by virus from a high-speed pellet which depends on the addition of both surfactant and tRNA (Fig. 1). There is, however, an appreciable time-dependent background, which does not represent incorporation into endogenous nucleic acid bases, nor does it seem to decrease when rate-zonal purified virus is compared with the high-speed pellet from viraemic plasma. Because this background represents almost one-third of the measured incorporation, we have devised a column assay to isolate and identify the major radioactive nucleic acid components formed in the reaction.

The major radioactive peak in the column assay consists solely of N^2-methylguanine as identified in six thin-layer chromatography solvents (including isopropanol–HCl–water, 68 : 17.6 : 14.4, and n-butanol–water–ammonium hydroxide, 86 : 14 : 1) and ion exchange on 'Dowex 50' resin with known methylated bases (Fig. 2). The major nucleic acid hydrolysis products in this column assay elute in the following order: uridylic acid, cytidylic acid, guanine and adenine.

A comparison of the N^2-guanine methylase activity in virus from a high-speed pellet with the activity of rate-zonal purified virus from the same sample of viraemic plasma is shown in Table 1. There is only a modest increase in specific activity, which probably results from the high concentration of virus existing in the high-speed pellet; most cellular contaminants are removed by the previous centrifugation at 10,000*g* for 15 min. If methylase activity were adventitiously present, perhaps trapped in membrane vesicles formed from cell fragmentation, there should be a significant decrease in specific activity because there is considerable purification of AMV from these components by rate-zonal centrifugation. Our result therefore suggests that the enzymatic activity is associated with the virions. Table 1 also shows that the methylase activity is: (*a*) stable after multiple freezing and thawing in standard assay buffer; (*b*) destroyed by heating at 100° C for 3 min in standard assay buffer; (*c*) zero with *E. coli* DNA (200 µg, heat denatured); and (*d*) only one-eighth the amount of acceptance of methyl groups by an equivalent amount of brewer's yeast tRNA in the same conditions. Data from experiments not presented here indicate that the methylase activity is released by 'Nonidet-P40' (0.25% v/v), and that concentrations of 'Sterox SL' as high as 1% v/v do not cause inhibition of activity.

Fig. 3 is an electron micrograph of a typical preparation of rate-zonal purified AMV which shows the purity. Although only briefly described here, a more detailed report of this purification procedure will be published shortly (K. Stromberg, in preparation).

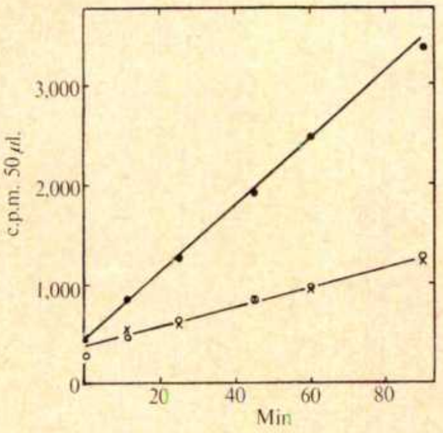

Fig. 1 Enzyme assay. The standard assay buffer contained 50 mM Tris HCl, *p*H 8.3, at 37° C, 60 mM NaCl, 16 mM magnesium acetate, 30 mM dithiothreitol. The incubation volume was 0.2 ml. containing 400 µg tRNA (*E. coli* B), 2.5 µCi S-adenosylmethionine-methyl-^{3}H (New England Nuclear Corp., specific activity 3.28 Ci/mmol) and 0.4 mg to 0.8 mg virus protein (Lowry procedure). The virus was disrupted by preincubation with 0.75% v/v 'Sterox SL', a nonionic surfactant (Monsanto Co.) in standard buffer at 0° for 15 min and an equal volume of the virus solution was added to the incubation solution to start the reaction. The radioactive incorporation was assayed by the filter paper technique of Mans and Novelli[7], in which the hot trichloroacetic acid extraction was omitted. ●, Complete incubation; ×, minus tRNA; ○, minus surfactant.

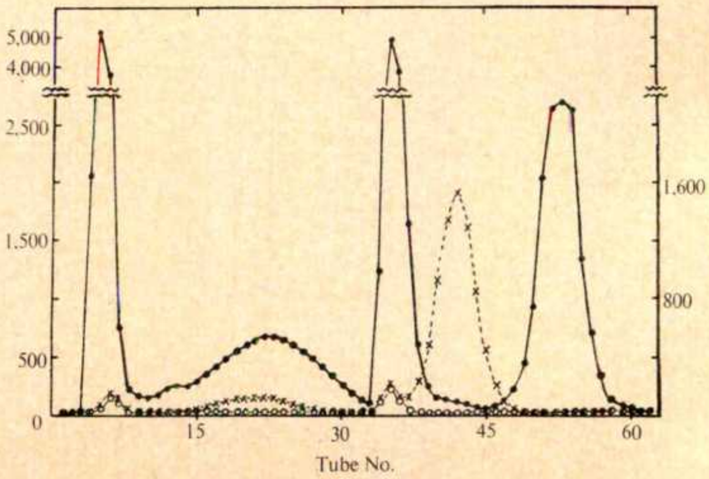

Fig. 2 Analysis of ^{3}H incorporation by hydrolysis and ion exchange chromatography. A sample of 2 ml. of 1 M Tris-HCl, *p*H 8.5, and 4 mg of carrier tRNA was added to the incubation solution and then precipitated in the cold with 1 ml. of 50% trichloroacetic acid. After centrifugation the pellet was suspended in 2 ml. of 1 M Tris-HCl and stirred for 20 min at room temperature. Undissolved material was removed by centrifugation and the supernatant was precipitated as above four times. After the final precipitation had been hydrolysed in 3 ml. of 1 N HCl at 97°–99° C for 30 min, it was applied to a 'Dowex 50-H$^+$' column (1 cm × 7 cm) equilibrated with 1 N HCl. Gradient elution was accomplished by mixing 2 M ammonium acetate with 125 ml. of 1 M acetic acid in a closed flask. Fractions containing 1.4 ml. were collected each 10 min, monitored at 260 nm and counted in 15% 'Biosolve'-toluene solution. ●, A_{260}; ×, ^{3}H in complete incubation; ○, ^{3}H in incubation minus tRNA.

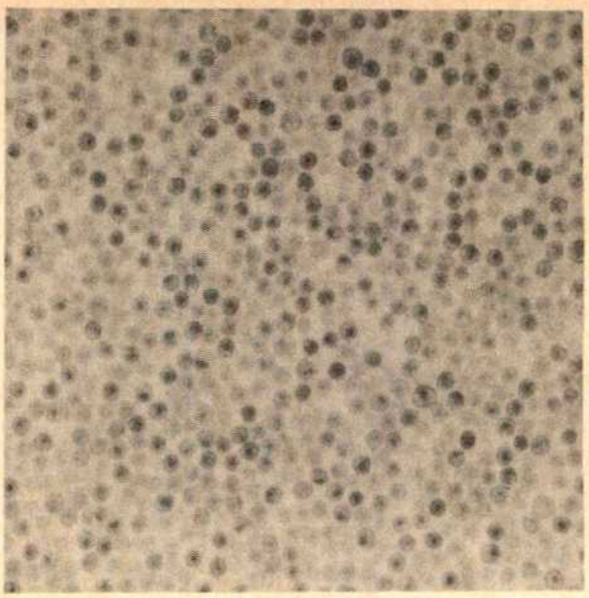

Fig. 3 Thin section electron micrograph of rate-zonal purified AMV. (× *c.* 20,000.) Viraemic plasma (from leukaemic chicks in which by microleucocrit at least 20% of the blood volume consisted of myeloblasts) was centrifuged at 5,000*g* for 15 min (low speed) and the supernatant solutions were pooled and centrifuged at 10,000*g* for 15 min (intermediate speed spin). Aliquots of this supernatant plasma were then layered on 'Ficoll' gradients (5%–25%) in the standard virus purification buffer (0.1 M NaCl, 1 mM EDTA sodium salt, and 50 mM Tris-HCl, with final *p*H of 7.4 at 0° C), and centrifuged at 25,000 r.p.m. for 55 min in 5/8 × 4 inch buckets in an SW27 rotor. The dense virus band below the 'Ficoll'-plasma interface was removed with a syringe by needle puncture, the pooled bands were diluted twice with standard buffer and centrifuged at 40,000*g* for 60 min. The resulting rate-zonal purified pellet was suspended in the methylase assay buffer. If the 'Ficoll' centrifugation procedure was omitted, the supernatant after the intermediate speed spin was pelleted by centrifugation at 40,000*g* for 60 min to give a high-speed pellet which was resuspended in the standard assay buffer. Note the absence of nonviral material.

Table 1 Response of Methylase Activity to Various Conditions

	Total c.p.m./h in N^2-methylguanine	Specific activity of methylase: c.p.m./mg protein/h
High-speed pellet virions:		
Complete incubation	19,300	24,400
Minus tRNA	0	
Frozen three times	20,800	26,300
Frozen five times	19,400	24,500
Plus yeast tRNA	2,520	3,180
Plus DNA	0	
Heat treated	0	
Rate-zonal purified virions:		
Complete incubation	17,620	28,900
Minus tRNA	0	

More than 90% of the detectable methylase activity is specific for N^2-methylguanine. Though this apparent specificity suggests that the activity might be an important function for the virus, complications are introduced by the complexities of the methyl acceptor (for example, unfractionated tRNA) and the variety of different conditions required for optimum activity of the various methylases[5]. As well as the possibility that this enzyme is important in the virus life cycle, its association with an oncogenic virus suggests a possible connexion with the aberrant methylation hypothesis of malignancy proposed by Srinivasan and Borek[6]. In this regard, it would be valuable to examine other RNA tumour viruses for a specific RNA methylase activity.

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Changes in Hepatic Nuclear DNA-dependent RNA Polymerase caused by Growth Hormone and Triiodothyronine

WHEN hypophysectomized rats are given growth hormone or triiodothyronine, the rate of RNA synthesis is accelerated, followed by that of protein synthesis and a resumption of growth[1,2]. The two hormones apparently affect the pattern of hepatic RNA synthesis in different ways[3,4] and we have now found that the two hormones affect the multiple RNA polymerases of isolated nuclei in different ways.

The existence of more than one RNA polymerase activity in isolated nuclei, involving the synthesis of ribosomal and non-ribosomal RNA, was inferred from experiments in which nuclei were incubated in high and low concentrations of salt[7]. After chromatographic separation[5,6] the enzymes have the ionic requirements for ribosomal (nucleolar) or non-ribosomal (nucleoplasmic) RNA formation. We have also made use of the ability of the fungal toxin α-amanitin to inhibit selectively the nucleoplasmic RNA polymerase activity[8,12].

Male Sprague Dawley rats (90–110 g) were hypophysectomized and maintained on standard laboratory chow supplemented by salt and sucrose. Seven and eight days later they were given either a single subcutaneous injection of 3,3′-5-triiodo-L-thyronine, 20–22 h before death, or received bovine growth hormone (from the National Institutes of Health, Bethesda) or human growth hormone (International Standard, National Institute for Medical Research, Mill Hill) 12 and 3 h before death, respectively. Nuclei were prepared from liver by differential centrifugation and their capacity to form RNA was measured *in vitro*[7,13]. The DNA-dependent RNA polymerases were isolated by chromatography on 'DEAE Sephadex'[5,6]. Enzyme activity was assayed and fractions corresponding to different peaks were pooled. Protein was assayed by the filter paper technique with xylene brilliant cyanin G staining[14].

The choice of the time of subsequent analysis was predicated from the results of previous experiments showing changing RNA polymerase activities and not necessarily maximal stimulation. In this way we hoped to select for the early responses to the hormone action. In the initial experiments RNA polymerase was measured in whole nuclei at low and high ionic strength and in the presence or absence of α-amanitin. There was significantly greater inhibition of ATP incorporation by α-amanitin at high than at low ionic strength with both control and hormone-treated animals; however, after injection of growth hormone, there was a significant reduction in inhibition of the enzyme assayed at low ionic strength (Table 1). The amanitin-insensitive enzyme is the more active when nuclei are assayed at low ionic strength with a preponderant synthesis of ribosomal RNA. The decreased inhibition by amanitin after treatment with growth hormone suggested more activity or a greater quantity of this type of enzyme, but did not indicate whether a change had occurred in the amanitin sensitive enzyme. Triiodothyronine enhanced sensitivity to α-amanitin assayed at low ionic strength. This observation is difficult to assess; it may indicate a greater representation of the "nucleoplasmic" enzyme in the conditions of assay.

The elution profile of enzymatically active fractions isolated from nuclei of liver from hypophysectomized animals resembles that from normal rat liver and consists of three separate peaks of activity (Fig. 1*a*). The first peak eluted from the column (peak A) has been observed before it is eluted after the bulk of the protein, with the 0.1 M ammonium sulphate buffer wash, and is probably a complex mixture of proteins including RNA polymerase enzymes. Preliminary observations show that it is insensitive to rifamycin; inhibited by 3–5% by α-amanitin (2 μg/ml.), at which concentration the activity of the second peak (B) is inhibited by 3% and that of the last major peak (C) inhibited by 90%; possesses DNAase-like activity towards

Table 1 Differential Inhibition by α-Amanitin of Stimulation of RNA Polymerase in Whole Nuclei by Growth Hormone and Triiodothyronine administered to Hypophysectomized Rats

Treatment	0.3 M $(NH_4)_2SO_4$ added	Incorporation of ATP (pmol/mg DNA/10 min)	% inhibition by α-amanitin
None	−	193	17
	+	305	69
200 μg BGH; 10 h	−	237	10
	+	536	63
20 μg T_3; 22 h	−	229	29
	+	412	68

Nuclei were isolated from livers of three rats following administration of 0.15 M NaCl (control) or hormone as indicated. The nuclei were incubated as described[7] in the presence or absence of added ammonium sulphate. Each experiment was repeated at least twice. The α-amanitin concentration was 2 μg/ml.

Table 2 Specific Activities and Hepatic Concentrations of DNA-dependent RNA Polymerase isolated from Nuclei of Control (Untreated) and Hormone Treated Hypophysectomized Rats

	Incorporation of ^{3}H-UTP (nmol/mg protein/30 min)						µg protein/g wet weight liver		
Enzyme	Hypex	% inhibition by α-amanitin	Hypex+ HGH	% inhibition by α-amanitin	Hypex+ T_3	% inhibition by α-amanitin	Hypex	Hypex+ T_3	Hypex+ HGH
A	1.02	3	0.985	3	1.83	4	35.7	47.0	128.0
B	0.967	3	0.900	0	1.15	5	31.4	24.8	46.0
C	42.0	95	36.0	97	27.4	92	6.77	7.70	6.30

Nuclei were isolated from 30–35 g (six to eight rats) of rat liver following 0.15 M NaCl or hormone treatment as indicated in the text. RNA polymerase was isolated by a modification of the method described by Roeder and Rutter[5] and after overnight dialysis was applied to DEAE-'Sephadex' columns. The various enzymes were eluted with 0.1 M $(NH_4)_2SO_4$, 0.05 M Tris *p*H 7.4, 5 mM $MgCl_2$, 0.5 mM dithiothreitol, 0.1 mM EDTA, 20% glycerol wash followed by a 0.1–0.5 M $(NH_4)_2SO_4$ gradient in the same buffer. The column eluate was assayed as indicated in Fig. 1. The peaks of activity were reassayed and pooled. Protein concentrations and content and α-amanitin sensitivity were determined on each enzyme peak. Each experiment was repeated at least twice, and each determination was carried out in triplicate. The α-amanitin concentration was 5 µg/ml.

adenovirus DNA and no lytic activity towards bacterial 16S ribosomal RNA or to polyadenylic acid (unpublished results of E. A. S. and W. C. Russell). There is a significant and selective change in the properties of this fraction following hormonal treatment.

Triiodothyronine did not change the elution profile pattern of peaks B and C, nor their sensitivity towards α-amanitin, but increased slightly the activity in peak A (Fig. 1*c*). After treatment with growth hormone, there was a striking increase in the activity in peak A (Fig. 1*b*). There was little change in specific activities of the pooled enzymes in peaks A, B and C after growth hormone treatment, but triiodothyronine increased the specific activity of A and slightly decreased that of B (Table 2). The recovery of total protein per gram wet weight of liver increased remarkably in peak A after treatment. These results are consistent with the assay of whole nuclear preparations and show that the principal change occurs in the amanitin resistant enzyme activity.

We think that these changes represent subtle hormone-specific modifications of hepatic nuclear RNA polymerase activity before an enhanced rate of protein synthesis. The nature of the enzyme activity in peak A is not clear, but administration of growth hormone is associated with significant increases in the total protein content of peak A with maintenance of its specific activity, suggesting an increased concentration of this

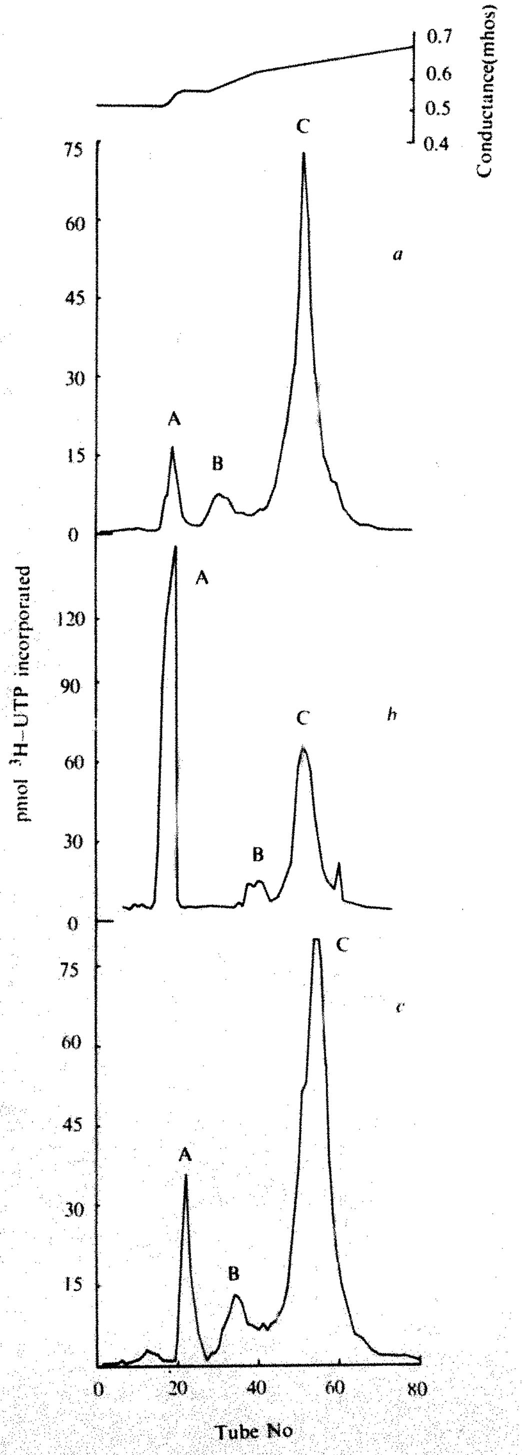

Fig. 1 Elution profiles of RNA polymerase isolated from the livers of (*a*) hypophysectomized rats, (*b*) hypophysectomized rats treated with human growth hormone, and (*c*) hypophysectomized rats treated with triiodothyronine. Nuclear RNA polymerase, isolated by a modification of the procedure described by Roeder and Rutter[5], was dialysed overnight at 0° C against 0.05 M $(NH_4)_2SO_4$ in 0.05 M Tris (*p*H 7.4 at 20° C), 5.0 mM $MgCl_2$, 0.5 mM dithiothreitol, 0.1 mM EDTA, 20% glycerol. After dialysis the suspension was centrifuged at 105,000*g* for 1 h. The clear faint yellow supernatant was applied to a 0.9×25 cm DEAE-'Sephadex' column, washed into the resin with 10 ml. of 0.05 M $(NH_4)_2SO_4$ in the same buffer (with which the bulk of the protein was eluted), followed by 10 ml. of 0.1 M $(NH_4)_2SO_4$ (which eluted a peak of enzyme activity (A), especially after growth hormone), and then with a linear 0.1-0.5 M $(NH_4)_2SO_4$ gradient. Each fraction (0.75 ml.) was assayed for ^{3}H-UTP incorporation with 0.8 mM ATP, GTP, and CTP, 7 µM-^{3}H-UTP, 86 mM Tris (*p*H 8.3 at 37°), 8% glycerol, 29 µM EDTA, 140 µM, dithiothreitol, mM KCl 57 120 µg/ml. calf thymus DNA, 2 mM $MnCl_2$, with the ammonium sulphate concentration at elution. After 20 min of incubation at 37° C, aliquots were pipetted onto 2.4 cm No. 1 Whatman disks, which were processed by washing first in 10% trichloroacetic acid (TCA) and 1% sodium pyrophosphate at 0° C, twice in 5% TCA and 1% sodium pyrophosphate, twice with 95% alcohol, once with absolute alcohol, once with alcohol : ether (1 : 1 v/v), and once with ether[15]. The radioactivity in the dried disks was measured in 0.05% 1,4-bis (2-(4-meth-5-phenyloxazolyl)) benzene with 0.4% 2,5-diphenyloxazole in toluene in a liquid scintillation spectrometer. The efficiency of counting was 6.8% with the method employed. Conductance was measured with a Phillips conductivity meter, with values given in mmhos.

form of polymerase. The material in peak A is not homogeneous and might be the same, amanitin-resistant, enzyme which appears in peak B; hormonal treatment could have caused some of the enzyme in peak B to be eluted at a lower ionic strength. The absence of change in specific activity in peak A in the face of an increased protein content of peak A without significant changes in B suggests that more than a redistribution of the enzyme has occurred. No significant alteration in peak C activity was associated with growth hormone therapy. Triiodothyronine administration, on the other hand, enhanced both the quantity and the specific activity of peak A, the former to a very minor degree, the latter significantly. Interpretation of specific activities and enzyme yields is complicated; although recovery of enzyme activity after chromatography was of the order of 70–80% of the starting material we have not checked for possible enhanced differential enzyme extraction brought about by hormonal stimulus under identical experimental circumstances. These results indicate that treatment with growth hormone is followed by the accumulation of more amanitin-resistant enzyme with different elution behaviour from enzyme B, and that triiodothyronine enhances the specific activity of this same enzyme. Whether the altered elution properties are related to new enzyme formation, to direct hormone interaction with pre-existing enzyme, or to a functional modification of the enzyme awaits further study.

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Effect of Steroids and Dibutyryl Cyclic AMP on the Sensitivity of Haemopoietic Stem Cells to ^{3}H-Thymidine *in vitro*

AN early action of testosterone and chemically related steroids is to increase the sensitivity of spleen colony forming units (CFU) to the cytocidal action of high specific activity ^{3}H-thymidine[1]. This can be observed as early as 6 h after a single subcutaneous injection of steroid. CFU of normal adult miec are generally insensitive to the killing action of ^{3}H-thymidine[2]; hence the effect of steroids was interpreted as either triggering CFU from a resting (G_o) stage into cell cycle, or shortening the cell cycle of CFU.

Experimental polycythaemia, which reduces the level of endogenous erythropoietin, did not block the effect of testosterone propionate on CFU. Accordingly, it was concluded that erythropoietin was not required for the steroid action on the cell cycle of CFU.

The effect of steroids on CFU *in vivo* was observed 6 h after the subcutaneous administration of poorly soluble compounds suspended in an aqueous medium, so that the effect following absorption may be more rapid. This study was designed, in part, to determine whether testosterone given *in vitro* could increase the sensitivity of CFU to ^{3}H-thymidine.

Adenosine-3′ : 5′-monophosphate (cyclic AMP) is thought to act as a "second messenger" for a variety of hormone end-effects[3,4]. While the "second messenger" concept may be applied to many of the polypeptide hormones and to catecholamines, evidence does not strongly support its application to steroid hormone action. Accordingly, steroids and cyclic AMP may produce similar biological end-effects by acting through different cellular mechanisms[5]. To test whether it might mimic any effect of testosterone on CFU, the ability of its dibutyryl derivative to change the sensitivity of CFU to ^{3}H-thymidine was studied.

$C_3H \times AKR$ female mice served as both donors and recipients of bone marrow cells; mice were 9–11 weeks old. The steroids studied were testosterone hydrogen succinate (THS), a water soluble compound, and 5β-dihydrotestosterone (5β-DHT). THS was studied over a range of 2.4×10^{-14}–2.4×10^{-6} M and 5β-DHT at 10^{-8} M; the required amount of 5β-DHT was added dissolved in 1 μl. of 95% ethanol. Dibutyryl cyclic AMP was studied over a range of 10^{-14} to 10^{-6} M; as a control for dibutyryl cyclic AMP, adenosine-5′-monophosphate (5′-AMP) was studied over the range of 10^{-10} to 10^{-6} M. 5′-AMP is the principal product of the breakdown of cyclic AMP by 3′:5′-mononucleotide phosphodiesterase.

Cultures of bone marrow cells (1.6 ml. 4–5.5×10^6 cells/ml.) suspended in Fischer medium at *p*H 7.4 were incubated at 37° C in a shaking water bath. From 0–2.5 h, cultures were treated with various concentrations of the agents described above; at 2.5 h, the culture volumes were increased to 2.0 ml. by the addition of 0.4 ml. of pre-warmed Fischer medium with or without 400 μCi of ^{3}H-thymidine (22 Ci/mmol). After 0.5 h exposure to ^{3}H-thymidine, the cultures were diluted approximately 1:13 with cold Fischer medium; 0.25 ml. of diluted suspension was injected intravenously into irradiated (850 rad) recipients. Groups consisted of twelve to fifteen mice. Spleen colonies[6] were counted 9 days after transplantation. The percentage loss of CFU from cultures due to ^{3}H-thymidine was estimated. During culture, untreated CFU do not increase their sensitivity to ^{3}H-thymidine.

Fig. 1 shows the effect after 3 h of THS and of 5β-DHT on the sensitivity of CFU to ^{3}H-thymidine; both agents increased ^{3}H-thymidine sensitivity. The effect after 3 h of dibutyryl cyclic AMP and of 5′-AMP is shown in Fig. 2. While dibutyryl cyclic AMP increased the sensitivity of CFU, 5′-AMP was relatively ineffective. The dose-response curve to dibutyryl-cyclic AMP is bell-shaped. Peak effect is seen at about 10^{-8} M; at 10^{-6} molar, however, the ^{3}H-thymidine effect is lost.

These results indicate that, given *in vitro*, THS, 5β-DHT, and dibutyryl cyclic AMP increase the sensitivity of CFU to the cytocidal action of ^{3}H-thymidine within 3 h; these agenst presumably trigger CFU into cell cycle or shorten their cell cycles. Preliminary studies suggest that THS and dibutyryl cyclic AMP increase the ^{3}H-thymidine sensitivity of CFU as early as 1 h after exposure in bone marrow cells.

The effectiveness of the testosterone derivatives in a system free of either plasma or serum strengthens the suggestion that the previously reported[1] effect of steroids on the sensitivity of

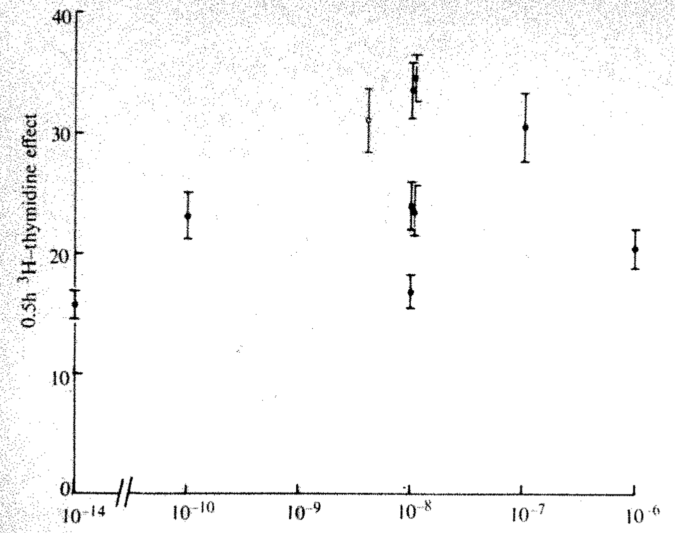

Fig. 1 Effect of testosterones on CFU *in vitro*. ●, Testosterone hydrogen succinate; ○, 5β-dihydrotestosterone.

CFU to ^{3}H-thymidine *in vivo* does not require the presence of erythropoietin or any other plasma macromolecule. This provides support for a direct action of testosterone on bone marrow CFU; there is further confirmation for the haemopoietic activity of steroids with the 5β-H configuration[7-9].

The mechanism of action of the testosterones on the cell cycle of CFU is not clear. Recent studies on the binding of steroids to specific cytoplasmic receptors, followed by the migration and subsequent combination of this complex with specific receptors in the nucleus[5], offer a possible approach to this problem.

The effectiveness of dibutyryl cyclic AMP within the range of physiological concentrations of cyclic AMP found in several tissues[10] suggests that the adenyl cyclase system plays a role in regulating the proliferative state of CFU. This view is further supported by recent studies from our laboratory[11] which demonstrate that low concentrations (less than 10^{-12} M) of isoproterenol (isoprenaline), a stimulant of β-adrenergic receptors, also act to trigger CFU into cell cycle. This effect is blocked by propranolol, a compound which specifically blocks β-adrenergic receptors. β-Adrenergic activity is closely associated with the adenyl cyclase system. The presence of such a receptor presumably on the cell surface of CFU, and the capacity of this receptor when activated to initiate DNA synthesis, argues for the regulatory role of the adenyl cyclase system. Until cell separation techniques permit a more direct investigation of biochemical events within CFU, this suggestion must remain speculative.

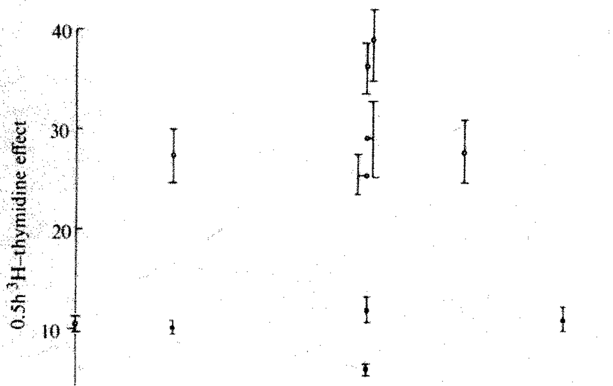

Fig. 2 Effect of cyclic AMP on CFU *in vitro*. ●, 5′-AMP; ○, dibutyryl cyclic AMP.

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Carcinogenic Hydrocarbons and Human Cells in Culture

BOYLAND[1] has suggested that 90% of cancer in man is caused by chemicals, either endogenous or environmental. The association of human cancer with hydrocarbons dates from Percival Pott's description of chimney sweeps' cancer in 1775, greatly reinforced by the isolation 150 yr later of benzo(*a*)pyrene from coal tar by Kennaway[2] and his associates[3]. Although there are probably many unidentified carcinogens in soot and coal tar, the correlation between the experimental production of cancer in animals with pure hydrocarbons and the incidence of cutaneous cancer in people exposed to tar, pitch, soot, oil and similar industrial products[4] is suggestive. It is much more difficult to assess the relevance of hydrocarbons to human cancer at other sites, and, in particular, their role in the induction of lung cancer remains unresolved.

In an earlier review[5] of chemical carcinogenesis it was suggested that interaction with nucleic acids was of primary importance, although at that time the only evidence of a positive nature that DNA was the essential cellular receptor for carcinogenesis was the correlation reported by Brookes and Lawley[6] between the carcinogenic potencies of a series of aromatic hydrocarbons and the extents to which these compounds were bound to the DNA of mouse skin *in vivo*. Since this time other positive correlations have been reported for alkylating agents, azo-dyes and hydrocarbons as discussed by Brookes and Dipple[7].

For a number of carcinogens, including the aromatic hydrocarbons, covalent binding to cellular macromolecules must involve a metabolite of the carcinogen. Diamond *et al.*[8] showed that the binding of 7,12-dimethylbenz(*a*)anthracene (DMBA) to the DNA, RNA and protein of cells in culture was much greater in normal rodent embryo cells than in transformed rodent cells and that this correlated both with the toxicity to, and much greater metabolism[9] by, normal as compared with transformed cells. Andrianov *et al.*[10] found that normal rodent fibroblasts metabolize benzo(*a*)pyrene (B(*a*)P) while transformed cells do not, again in agreement with the toxicity data. Duncan *et al.*[11] reported that although mouse embryo cells metabolize all the aromatic hydrocarbons tested, this metabolism leads to binding to cellular macromolecules only in the case of the carcinogenic compounds.

Previous studies[12,13] with hydrocarbons and human cells have been inconclusive because either neoplastic cells, or normal cells which had been in culture for a considerable length of time, were used. Prolonged culture is known to reduce the ability to bind DMBA even of rodent embryo cells[14]. In the experiments reported here the effects of carcinogenic hydrocarbons on primary human embryo cells have been examined and compared with their effect on human tumour cells (HeLa).

Human embryo fibroblast cultures were prepared from lung, skin/muscle and gut tissues and tested for their ability to metabolize and bind ^{3}H-labelled B(*a*)P and DMBA while similar studies were carried out with HeLa cells. In all cases the methods used were those described before[11].

Sterile tissue samples from 4–5 month human embryos were used to prepare lung, skin/muscle and gut fibroblast cultures (supplied by Dr H. E. M. Kay and the staff of the Foetal Tissue Bank of the Royal Marsden Hospital, London). Primary cultures were treated with ^{3}H-B(*a*)P and ^{3}H-DMBA as described previously[11] for mouse embryo cells. As Fig. 1 shows, both hydrocarbons were metabolized, DMBA rather more slowly than B(*a*)P. Calculation of the actual amount of B(*a*)P metabolized by the different cells in relation to the number treated gave the data of Table 1, which also includes the values obtained with cells which had been in culture for about 40 days (that is, at the tenth passage for the lung and skin/muscle cells and the seventh passage for the slower growing gut fibroblasts). It is apparent that the lung cells metabolize most efficiently and retain this property during subculture. On the other hand, the cells from the gut have a significantly poorer rate of metabolism after 40 days in culture.

The binding of B(*a*)P and DMBA to DNA, RNA and protein of the primary lung cells was determined after isolation of these cellular macromolecules. From these results (Table 2), binding indices were calculated and compared with corresponding values found previously for mouse embryo cells[11] (Table 3).

These results establish that in human embryo cells, the rate of hydrocarbon metabolism is similar to that in rodent embryo cells, and that at least for B(*a*)P, binding to macromolecules is also similar (Table 3). In the case of DMBA, the binding index, although of the same order as for B(*a*)P (Table 3), is significantly less than the very high value obtained previously with mouse embryo cells.

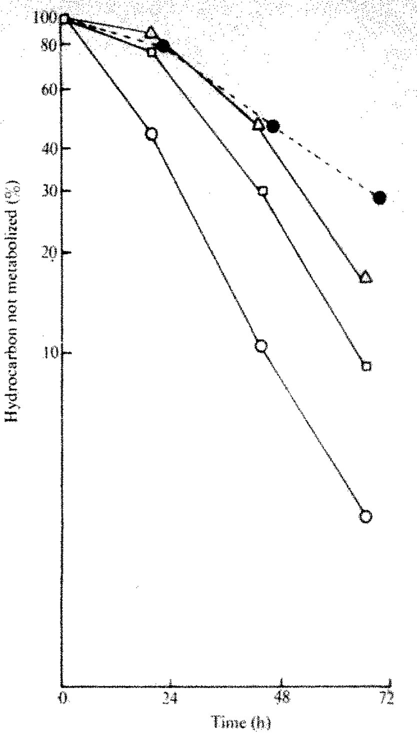

Fig. 1 The time course of metabolism of ^{3}H-B(*a*)P by primary human embryonic lung (○), gut (□) and skin/muscle (△) fibroblasts, and of ^{3}H-DMBA by primary human embryonic lung cells (●). The cell cultures were prepared by trypsinization of tissues from 4–5 month human embryos. Approximately 2×10^{6} cells were plated in 4 oz medical flat bottles containing 15 ml. of Eagle's medium (MEM, Cat. No. F11, Grand Island Biological Co., New York) supplemented with 15% foetal calf serum (Flow Laboratories Ltd, Irvine, Scotland). The cells were treated 3 days later with randomly tritiated B(*a*)P (specific activity 5.8 Ci/mmol) or DMBA (specific activity 17 Ci/mmol) in dimethylsulphoxide (final concentration 0.5%). Metabolism was followed by extraction of 1 ml. of medium with 5 ml. of cyclohexane at zero time and subsequently, as described previously[15]. The initial concentration of B(*a*)P was 0.26 μM and of DMBA 0.10 μM.

Table 1 Metabolism of ^{3}H-B(*a*)P by Cultures of Fibroblasts derived from Various Human Embryonic Tissues

Cell type	Number of cells per bottle: Primary culture	Number of cells per bottle: After 40 days in culture	Total B(*a*)P metabolized (nmol): Primary culture	Total B(*a*)P metabolized (nmol): After 40 days in culture	Amount B(*a*)P metabolized per 10^{6} cells (nmol): Primary culture	Amount B(*a*)P metabolized per 10^{6} cells (nmol): After 40 days in culture
Lung	1.9×10^{6}	1.8×10^{6}	3.8	4.0	2.0	2.2
Skin/muscle	2.9×10^{6}	1.3×10^{6}	3.3	1.7	1.1	1.0
Gut	2.0×10^{6}	1.3×10^{6}	3.6	0.75	1.8	0.58

The cells were tested after either 4 days (primary cultures) or 40 days in culture. The cells wre prepared and treated essentially as described in Fig. 1. The metabolism figures given were obtained after 72 h exposure to ^{3}H-B(*a*)P (0.26 μM). The extent of metabolism was estimated as described in Fig. 1 and the final number of cells was determined by trypsinization and counting in a haemocytometer.

Table 2 Extent of Reaction of ^{3}H-B(*a*)P and ^{3}H-DMBA with Cellular Macromolecules of Primary Human Embryonic Lung Cells

Hydrocarbon	Concentration of hydrocarbon in medium (μM)	Time of treatment (h)	% HC metabolized	Extent of binding to macromolecules: μmol/mol P DNA	Extent of binding to macromolecules: μmol/mol P RNA	Extent of binding to macromolecules: μmol/100 g protein
Benzo(*a*)pyrene	0.28	48	84	3.04	5.60	1.03
	0.31	48	78	3.69	6.44	3.65
7,12-Dimethylbenz(*a*)-anthracene	0.10	96	77	1.40	1.08	0.51
	0.10	96	82	1.66	1.14	0.44

Cells were prepared as outlined in Fig. 1 except that approximately 2×10^{7} cells were plated in large flat glass bottles (Thompson bottles, Gallenkamp & Co Ltd, London) containing 150 ml. of Eagle's medium. After the time stated, cellular macromolecules were isolated and assayed for bound radioactivity as described[8].

Table 3 Binding Indices of B(*a*)P and DMBA obtained with Primary Human Embryonic Lung Cells

Hydrocarbon	Binding index, μmol/mol P (or μmol/100 g for protein) divided by nmol/ml. metabolized					
	Human embryo lung			Mouse embryo		
	DNA	RNA	Protein	DNA	RNA	Protein
Benzo(*a*)pyrene	12.7	23.4	4.3	18.5	15.5	12.0
	15.4	26.8	15.2	13.0	17.0	11.0
7,12-Dimethylbenz(*a*)anthracene	18.2	14.0	6.6	170	130	22
	20.8	14.3	5.5	209	144	26

The binding indices represent the extent of reaction of the hydrocarbon with the particular macromolecule resulting from the metabolism of 1 nmol of hydrocarbon per ml. of medium to which the cells were exposed. They are calculated from the data of Table. 2 Also given are the values found for mouse embryo cells in similar experiments.

Table 4 Metabolism and Binding of ^{3}H-B(*a*)P and ^{3}H-DMBA to Monolayer Cultures of HeLa Cells

Hydrocarbon	Concentration of hydrocarbon at zero time (μM)	% conversion to water soluble form at time stated				Binding index, nmol/mol P (or μmol/100 g for protein) divided by μmol/ml. metabolized		
		Zero	24 h	48 h	72 h	DNA	RNA	Protein
Benzo(*a*)pyrene	0.28	Nil	48	68	82	5.4	7.1	5.7
7,12-Dimethylbenz(*a*)anthracene	0.17	Nil	26	35	47	18.8	15.9	5.0

The metabolism experiments were performed essentially as outlined in Fig. 1. After 72 h cellular macromolecules were isolated, the extent of hydrocarbon binding determined and the binding indices calculated as described previously[11].

Similar metabolism and binding experiments were carried out with monolayer cultures of HeLa cells (Table 4). As with the primary human embryo cells both B(*a*)P and DMBA were metabolized, but the DMBA metabolism was considerably slower. The resulting macromolecular binding as indicated by the binding indices can be compared with the values obtained with the embryo cells (Table 3). While the binding of B(*a*)P to DNA, RNA and protein was significantly less in HeLa cells than in primary human lung cells, the binding of DMBA was very similar in both cell types.

It has been suggested[15] on the basis of detailed studies of B(*a*)P metabolism in mouse embryo cells that alternative pathways of hydrocarbon metabolism may exist, only one of which results in macromolecular interaction. The results discussed above could be explained if HeLa cells are defective in the enzyme system leading to binding, and studies of the pattern of B(*a*)P metabolites produced by HeLa as compared with embryo cells might indicate whether this is the case. DMBA binding in both HeLa and human embryo lung cells is considerably lower than that in mouse embryo cells, and this again may indicate different pathways of metabolism of this hydrocarbon by different cell types.

Preliminary experiments indicate the need for caution in interpreting toxicity data. Neither B(*a*)P nor DMBA affected the plating efficiency of HeLa cells over a concentration range of 0.05–50 nmol/ml. of medium, but the size of the colonies decreased with increasing dose. An effect consistent with these observations was seen when HeLa cells in suspension were treated with hydrocarbons. After 24 h in these conditions the cell number relative to control decreased with increasing hydrocarbon concentration.

This pattern of toxicity response by HeLa cells is in contrast to that found for rodent embryo cells (unpublished data) where a reduction in plating efficiency was evident at the lowest dose used (0.05 nmol/ml.) while no effect on colony size was apparent even at the highest dose of hydrocarbon (50 nmol/ml.).

It is becoming accepted[16] that any agent which is of itself an electrophilic reactant or is capable of being converted to such *in vivo*, and can therefore react with nucleophiles in the cell, is a potential carcinogen. For the aromatic hydrocarbons this would seem to depend on the structure of the metabolically produced ultimate carcinogen[17] and on the ability of a particular cell to generate this species.

The data reported in Table 3 indicate that, at least for B(*a*)P, primary human lung cells resemble mouse embryo cells in the degree to which the carcinogen becomes bound to cellular macromolecules following metabolism. The susceptibility of the mouse to hydrocarbon carcinogenicity is well established, and a correlation between hydrocarbon–DNA binding and carcinogenic activity has been found in the mouse skin[6]. Furthermore, several reports of transformation of mouse and hamster cells in culture by hydrocarbons have appeared[18–20] and the transformed cells have been shown to produce tumours when injected into adult animals. Our experiments suggest that the necessary conditions exist for the transformation of human lung cells by B(*a*)P.

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Antileukaemic and Nephrotoxic Properties of Platinum Compounds

THE antitumour properties of certain inorganic platinum compounds in mice were first reported by Rosenberg *et al.*[1]. Of thirty-four compounds tested the *cis*-platinum (ii) diamminodichloride and the *cis*-platinum (iv) diamminotetrachloride had the highest activity, producing marked regression of large solid sarcoma 180 tumours in 63–100% of mice.

In the rat we have found that the *cis*-platinum (ii) diamminodichloride and the *cis*-platinum (iv) diamminotetrachloride have strong antileukaemic effects on myeloid and lymphatic leukaemias. Although their effect is accompanied by uraemia, these two compounds seem to be superior to those in clinical use in that they have no undesirable effects on the normal cells of the marrow, gonads and intestine. Their antileukaemic and nephrotoxic properties seem to be related to the molecular configuration of the platinum compounds because the *trans*-platinum (ii) diamminodichloride and the *trans*-platinum (iv) diamminotetrachloride had no effect on either type of rat leukaemia nor on the kidneys of mice, rats or marmosets.

Specific pathogen-free mice and rats (Alderley Park Colony) were used. Myeloid and lymphatic leukaemias were induced in rats by feeding them with ICI 42,464 (2γ-chlor-β-isopropylamine) ethylnaphthalene hydrochloride). Litters less than 24 h old were injected intraperitoneally with whole blood from the dosed rats with either lymphatic or myeloid leukaemias[3]. After 4–6 weeks leukaemias were established in the injected newborn rats which had white cell counts of 30,000 to 110,000 cm^3.

Each platinum compound was administered intraperitoneally in a ball milled suspension in dispersol. Groups of six rats with myeloid leukaemias and six rats with lymphatic leukaemias received each compound in daily doses of 2 mg/kg, 0.5 mg/kg and 0.1 mg/kg. As controls, six rats with myeloid leukaemia and six rats with lymphatic leukaemia from the same transplanted litters were left untreated. Groups of six normal mice and six normal rats received *cis* $(NH_3)_2PtCl_2$, *trans* $(NH_3)_2PtCl_2$, *cis* $(NH_3)_2PtCl_4$ and *trans* $(NH_3)_2PtCl_4$ in daily doses of 4.0 mg/kg, 2.0 mg/kg, 1.0 mg/kg, 0.5 mg/kg and 0.1 mg/kg. Three groups consisting of two male and two female rats were given a single intraperitoneal dose of *cis* $(NH_3)_2PtCl_2$ at 5 mg/kg, 10 mg/kg and 20 mg/kg. Two normal male marmoset monkeys were given daily intraperitoneal injections of 2 mg/kg *cis* $(NH_3)_2PtCl_2$ and two normal male marmosets received 2 mg/kg daily of *trans* $(NH_3)_2PtCl_2$.

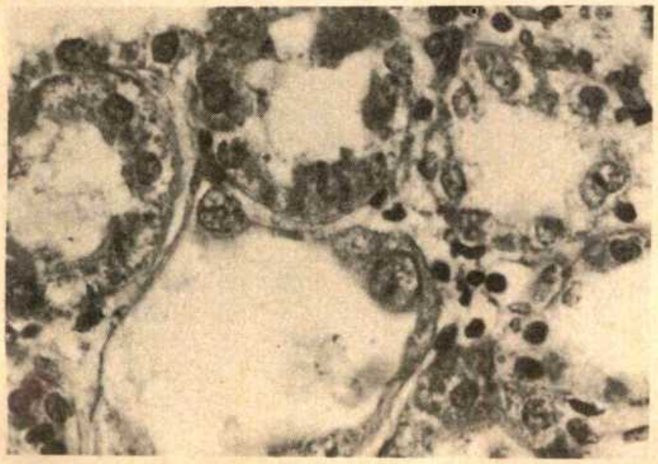

Fig. 1 Proximal convoluted tubules in rat after 5 days' treatment with 2 mg/kg *cis* $(NH_3)_2PtCl_2$ showing degeneration and necrosis of the epithelial cells (blood urea 145/mg%).

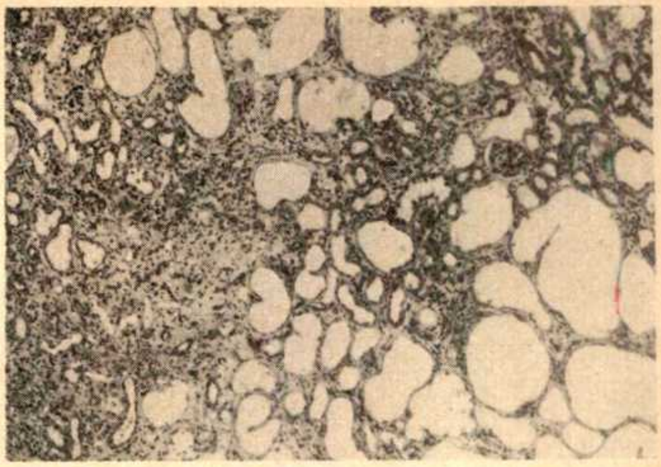

Fig. 2 Proximal convoluted tubules in rat after 5 days' treatment with 2 mg/kg *cis* $(NH_3)_2PtCl_2$ showing dilated tubules, atrophic epithelium, intertubular oedema and lymphocytic infiltration.

In normal mice and rats the *trans* $(NH_3)_2PtCl_2$ and the *trans* $(NH_3)_2PtCl_4$ produced no undesirable symptoms and the blood counts and the blood ureas remained within normal limits during the 24 days of dosing. At necropsy, histological examination revealed no abnormalities. Marmoset monkeys were unaffected by *trans* $(NH_3)_2PtCl_2$.

When *cis* $(NH_3)_2PtCl_2$ and *cis* $(NH_3)_2PtCl_4$ were given to normal mice and rats in a dose of 4 mg/kg a day, all animals died within 10 days; given 2 mg/kg a day, no animals survived after day 26. Haemoglobins, packed cell volumes, white cells, platelets and differential white cell counts were normal throughout the 24 days of dosing. Post mortem examinations showed the kidneys to be green and swollen and the corticomedullary regions to be congested. When examined by microscopy the kidneys showed degeneration and necrosis of the epithelium of the proximal convoluted tubules (Figs. 1 and 2). In mice and rats a renal tubular necrosis was seen in all animals dosed with 4 mg/kg and 2 mg/kg, but animals which received 0.5 mg/kg and 0.1 mg/kg did not develop a renal lesion and the blood ureas remained normal. The blood urea levels and the degree of tubular change in normal rats are shown in Table 1. Those of the mice were essentially the same. Rats given a single intraperitoneal injection of *cis* $(NH_3)_2PtCl_2$ at 5 mg/kg, 10 mg/kg and 20 mg/kg developed uraemia after 7–10 days (blood ureas 82, 167 and 167 mg/100 ml.) and the kidneys showed necrosis of the proximal convoluted tubules.

Marmoset monkeys given 2 mg/kg of *cis* $(NH_3)_2PtCl_2$ each day developed uraemia after 5–7 days (blood ureas 212 and 190 mg/100 ml.) and their kidneys showed a severe necrosis of the epithelium of the proximal convoluted tubules. Marmosets given *trans* $(NH_3)_2PtCl_2$ did not develop uraemia and their kidneys appeared histologically normal.

To assess possible beneficial effects of the platinum compounds on both myeloid and lymphatic leukaemias in the rat, the survival times of treated and untreated leukaemic rats and the effects on the white cell counts in the treated and untreated leukaemic rats were compared. The *cis* $(NH_3)_2PtCl_2$ and *cis* $(NH_3)_2PtCl_4$ were found to be equally effective against both myeloid and lymphatic leukaemias and the results of treating both types of leukaemia are therefore shown collectively. The

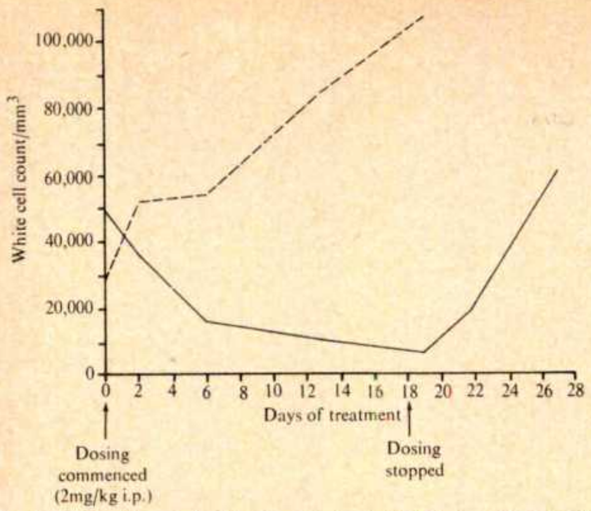

Fig. 3 Rats with myeloid leukaemia treated with *cis* $(NH_3)_2PtCl_2$. ——, 6 treated rats; ----, 6 untreated rats.

trans $(NH_3)_2PtCl_2$ and *trans* $(NH_3)_2PtCl_4$ were found to be completely ineffective in both types of leukaemia.

Leukaemic rats given 2 mg/kg of the *cis*-platinum compounds a day had reduced white cell counts, but uraemia developed and complicated the assessment of the survival times. The optimal daily dose of both the *cis* $(NH_3)_2PtCl_2$ and *cis* $(NH_3)_2PtCl_4$ for both types of leukaemia was 0.5 mg/kg and in this dose the blood urea concentrations were not increased and the convoluted tubules were histologically normal. The therapeutic toxicity ratio seems to be approximately 1:4.

The antileukaemic effects of both the *cis* $(NH_3)_2PtCl_2$ and the *cis* $(NH_3)_2PtCl_4$ seem to be very selective because in post-mortem and histological studies of leukaemic rats treated with 0.5 mg/kg daily, cytotoxic effects on the gonads, intestinal epithelium and the kidneys were not detected. The only effect of the *cis*-platinum compounds in rats dosed with 2 mg/kg seemed to be a slight blunting of the intestinal villi.

Both the *cis*-platinum compounds had a marked effect on the white cell counts and considerably prolonged the survival times of rats with both myeloid and lymphatic leukaemias (Table 2). When treatment with *cis* $(NH_3)_2PtCl_2$ was discontinued in the leukaemic rats there was an immediate and progressive increase in the white cell counts (Fig. 3). In no cases can it be said that a permanent cure was obtained.

We have compared our results with those we have obtained using antileukaemic drugs for the treatment of human leukaemias (Table 3). In rats, the effects of the *cis*-platinum compounds are very similar to those of asparaginase, corticosteroids and methotrexate.

Table 1 Effects of *cis* $(NH_3)_2PtCi_2$ and *cis* $(NH_3)_2PtCl_4$ on the Blood Ureas and Distal Convoluted Tubules of the Kidneys

Compound	Dose (mg/kg/day)	Blood ureas (mg per cent) Range	Mean	Effect on distal convoluted tubules
Cis $(NH_3)_2PtCl_2$	4.0	105–240	165	†††
	2.0	105–210	140	†††
	1.0	110–185	145	††
	0.5	39– 49	42	0
	0.1	34– 49	41	0
Cis $(NH_3)_2PtCl_4$	4.0	105–280	195	†††
	2.0	115–232	180	†††
	1.0	102–190	145	††
	0.5	35– 70	44	0
	0.1	31– 40	36	0
Normal rats	Undosed	25– 70	40	0

††† Dilatation of tubules, necrosis of epithelial cells and intertubular oedema and lymphocyte infiltration.

†† Degeneration of tubular epithelial cells but no obvious necrosis.

Table 2 Effects on the Survival Time and WBC of Dosing Rats with both Myeloid and Lymphatic Leukaemia with the Four Platinum Compounds (0.5 mg/kg daily)

Compound	Survival time (days) Range	Mean	Mean white cell counts/mm³ Before treatment	After treatment
Cis $(NH_3)_2PtCl_2$	12–48	32	64,000	4,000
Trans $(NH_3)_2PtCl_2$	2–14	6	42,000	180,000
Cis $(NH_3)_2PtCl_4$	10–34	24	82,000	11,000
Trans $(NH_3)_2PtCl_4$	4–12	9	74,000	220,000
Untreated leukaemic rats	4–18	8	30,000	110,000

Table 3 Effects on the Survival Times of Antileukaemic Compounds against Myeloid and Lymphatic Leukaemias in the Rat

Compound	Optimum dose (mg/kg)	Mean survival times (days) Lymphatic leukaemia	Myeloid leukaemia
Undosed leukaemic rats	—	7	9
Cis $(NH_3)_2PtCl_2$	0.5 i.p.	30	34
Cis $(NH_3)_2PtCl_4$	0.5 i.p.	25	23
Corticosteroids (paramethazone)	0.25 s.c.	44	11
Guinea-pig serum (asparaginase)	0.5 ml. i.p.	21	9
Methotrexate	0.25 i.p.	18	14

The antitumour properties of both *cis*-platinum compounds are of considerable interest because (1) they have a marked effect on sarcoma 180 and on both myeloid and lymphatic leukaemias in the rat; (2) they are virtually free from cytotoxic effects in normal haemopoietic tissue, the gonads and the intestinal epithelium; (3) they represent a new class of inorganic antitumour compounds, one in which molecular configuration seems to be critical for an effective antitumour result, for slight molecular rearrangement abolishes the antitumour effect; (4) being relatively simple inorganic compounds the relationship of chemical structure to antitumour properties should be more easily investigated and may perhaps lead to other chemical structures with similar or better antitumour properties; and (5) the antileukaemic effect of the *cis*-platinum compound seems to be closely related to the effect on the proximal con-

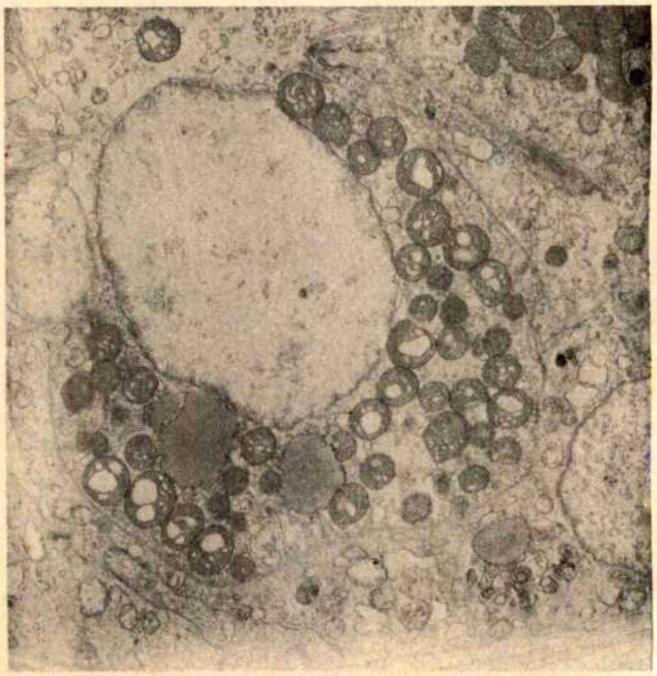

Fig. 4 Epithelial cell of distal convoluted tubule (×4,500), 48 h after a single intraperitoneal dose of 10 mg/kg of *cis* $(NH_3)_2PtCl_2$. The microchondrii have large vacuoles.

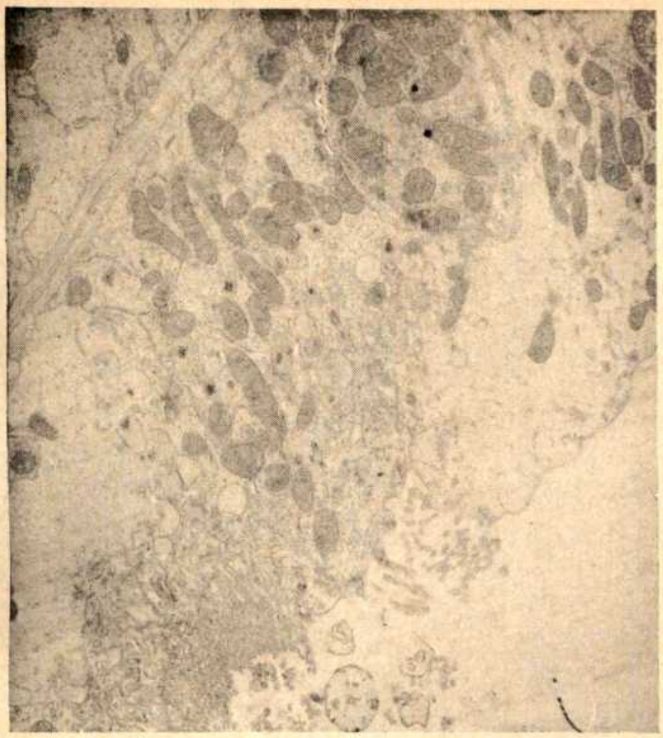

Fig. 5 Distal convoluted epithelium (×4,500) showing loss of brush border 72 h after a single intraperitoneal dose of 10 mg/kg of *cis* $(NH_3)_2PtCl_2$.

voluted tubules of the kidneys—both *cis*-platinum compounds have marked antileukaemic and nephrotoxic properties whereas the corresponding *trans*-platinum compounds possess neither of these properties.

The production of a necrosis of the proximal convoluted kidney tubules of rats and marmoset monkeys by *cis*-platinum compounds had not been reported before. This effect is very similar to those of mercurial compounds on man. By electron microscopy, we have tried to follow the development of the renal lesion in rats given a single 10 mg/kg intraperitoneal dose of *cis* $(NH_3)_2PtCl_2$. The first change, seen after 46 h, consisted of a marked vacuolation of the mitochondria of the epithelial cells of the proximal convoluted tubules (Fig. 4). This was followed after 72 h by a loss of the brush border (Fig. 5) and finally by complete disorganization and death of the tubular epithelial cells. No electron dense material suggesting platinum deposition in the tubular epithelial cells was seen.

The mode of action of *cis* $(NH_3)_2PtCl_2$ and $(NH_3)_2PtCl_4$ as potent antileukaemic compounds in the rat is of considerable interest, but it is not clear whether this is a direct and very selective effect on the tumour cells or whether the effect is indirect and perhaps mediated through the immunological system. The effects of *cis* $(NH_3)_2PtCl_2$ and *cis* $(NH_3)_2PtCl_4$ on rats with myeloid and lymphatic leukaemias justify a clinical trial of these compounds on human tumours and leukaemias. It seems that the most likely complication of such treatment would be uraemia due to acute tubular necrosis, but the safety margin is likely to be greater than that of conventional anti-tumour compounds.

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Photosynthesis and Gas Exchange of *Acetabularia* Chloroplasts in an Artificial Leaf

ISOLATED chloroplast preparations offer great advantages in the analysis of carbon pathways of photosynthesis because the system is not complicated by non-chloroplast metabolism, and kinetic analyses[1] can be made which are difficult with whole leaves[2]. Unfortunately the slow diffusion and equilibration of CO_2, HCO_3^- and CO_3^{2-} in the suspension medium is a serious disadvantage in gas exchange or $^{14}CO_2$–$^{12}CO_2$ pulse-chase experiments[3], but this difficulty can be overcome by using a thin film of concentrated chloroplast suspension spread on a non-absorbent support in the form of an "artificial leaf". Recent experiments by Coombs and Baldry have shown that pea and spinach chloroplast preparations supported on filter paper were stable only for periods of up to 10 min[4]. We have used *Acetabularia mediterranea* chloroplasts on filter paper to analyse the products of short term (1 s to 5 min) $^{14}CO_2$ fixation, but we found them insufficiently stable for longer experiments or gas exchange measurements. We have overcome this difficulty, however, by supporting chloroplasts on a non-absorbent grid instead of filter paper.

Acetabularia chloroplast preparations are made using mannitol isolating and suspending media[3] at *p*H 7.6. An artificial leaf is made by spreading a preparation containing 2 mg of chlorophyll/ml. evenly on a double layer of 74 mesh nylon bolting cloth stretched on a plastic frame. This is placed in a leaf chamber at 25° C in a closed circulating gas system with an infrared CO_2 analyser for gas exchange measurements[3]. The air entering the chamber is saturated with water and dried by a condenser before entering the CO_2 analyser. The humidifier contains distilled water and carbonic anhydrase; no measurable CO_2 absorption, retention or release occurs in the system lacking only chloroplasts. The size of the artificial leaf can be varied to suit experimental needs. Most experiments were done with a leaf of 6.5 cm diameter made with 0.50 ml. chloroplast suspension (about 15 µl./cm²).

Using this system photosynthesis begins immediately on illumination and reaches a maximum rate after a few seconds (Fig. 1). On darkening, CO_2 uptake stops abruptly and CO_2 evolution begins. Linear rates of CO_2 uptake or evolution can be maintained for at least 90 min. The CO_2 saturation curve for the artificial leaf is compared in Fig. 2 with that of chloroplasts in liquid system and intact cells in seawater. The three systems are quite similar, with CO_2 saturation occurring at approximately 0.18% CO_2 and compensation point at approximately 0.018% CO_2. Both saturation and compensation points are considerably higher than those usually found

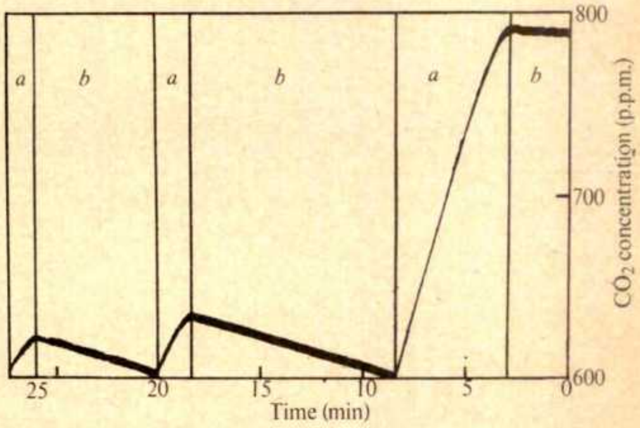

Fig. 1 A record of CO_2 exchange by an artificial leaf made with *Acetabularia* chloroplasts. O_2 content was 2%, light intensity 1,200 foot candles. The slopes correspond to rates of dark respiration of 5.1 µmol and photosynthesis of 72 µmol CO_2/h/mg chlorophyll. *a*, Light; *b*, dark.

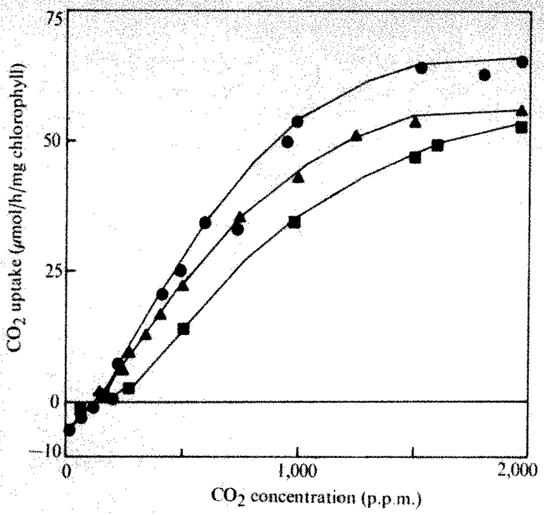

Fig. 2 The effect of CO_2 concentration on photosynthesis of chloroplasts in liquid medium (▲), of whole cells (■), and of the artificial leaf (●).

in leaves of higher plants. This presumably reflects the different CO_2 plus HCO_3^- concentration in the environment, the levels in seawater being several times higher than CO_2 in air. The effect of light intensity on photosynthesis is essentially similar in both the artificial leaf and in suspended chloroplasts (Fig. 3). Rates of CO_2 fixation by the artificial leaf up to two or three times higher than the rates in a liquid system have been observed using the same chloroplast preparation.

Table 1 Effect of O_2 Concentration on Dark Respiration, Photosynthesis and Photorespiration in an Artifical Leaf of *Acetabularia* Chloroplasts, as μmol CO_2/h/mg Chlorophyll

O_2 concentration	Dark respiration		Photosynthesis	Photorespiration in O CO_2
	after 30 min darkness	after 15 min illumination		
1.5	3.6	6.0	58	0
21	4.6	6.0	36	2.4
50	4.2	6.3	18	3.6

The effect of O_2 and CO_2 exchange in light and darkness is shown in Table 1. Photosynthesis is strongly inhibited and photorespiration is stimulated by O_2, as in the leaves of higher plants[5]. Dark respiration is unaffected by oxygen in the concentration range used. The fact that dark respiration increases after a period of photosynthesis confirms that recent photosynthate is a substrate[3].

The data of Coombs and Baldry[4] indicate that the density of pea or spinach chloroplast suspensions influences the pattern of photosynthetic carbon incorporation into intermediates.

Table 2 Distribution of ^{14}C among Products of 10 min Photosynthesis in $^{14}CO_2$ by Chloroplasts in Liquid Suspension, the Artificial Leaf, and Whole Cells of *Acetabularia*, as a Percentage of Total ^{14}C Fixed

Compound	Chloroplasts	Artificial leaf	Whole cells
Insoluble	54.7	55.2	61.7
Sugar diphosphates	0.6	0.5	2.3
Hexose monophosphates	3.3	0.9	1.1
Phosphoglyceric acid	2.5	1.0	11.1
Triose phosphates	0.7	0.5	0.5
Sucrose	14.4	18.9	7.9
Glucose	—	—	2.5
Glycolic acid	4.6	1.8	0.9
Aspartic acid	4.4	5.0	2.0
Glutamic acid	0.6	0.9	0.4
Serine	2.9	4.2	1.4
Glycine	2.1	1.1	2.1
Alanine	6.5	6.7	3.5
Malic acid	0.6	3.3	trace
Unidentified	2.1	trace	2.7

We have examined the incorporation of ^{14}C into the products of photosynthesis of *Acetabularia* using the artificial leaf, chloroplasts in liquid suspension and intact cells (Table 2). The chlorophyll content of the liquid system was 20 μg/ml. and of the artificial leaf was 2 mg/ml. In spite of the 100-fold difference in the ratio of chloroplasts to medium, there is very little difference in the pattern of distribution of ^{14}C in the products of photosynthesis of chloroplasts. The quantitative differences between the patterns for chloroplasts and whole cells are due in part to the difference between the *p*H of the suspending medium (7.5) and that of the cytoplasm (8.2–8.4)[6].

Table 3 Gas Exchange and Products of Photosynthesis by *Acetabularia* Chloroplast Preparations in ^{14}C-Bicarbonate (*p*H 8)

Gas exchange	μmol CO_2/h/mg chlorophyll	
	Crude preparation	Purified preparation
CO_2 uptake in light	52	45
CO_2 production in dark	12	7
Products of photosynthesis	^{14}C-content, % of total fixed in 10 min	
Insoluble products	20.4	25.1
Sucrose	8.9	9.1
Triose phosphate	1.1	1.2
Hexose monophosphate	5.6	8.3
Sugar diphosphate	11.0	7.4
Phosphoglyceric acid	6.9	5.0
Glycolic acid	23.3	21.3
Glyceric acid	0.7	0.5
Malic acid	0.9	0.3
Citric acid	0.1	0
Succinic acid	0.1	0
Alanine	3.9	7.5
Serine + glycine	12.9	11.4
Aspartic acid	3.6	2.4
Glutamic acid	0.6	0.5

The crude preparation was centrifuged only once (500*g*, 5 min) after isolation, and contained many large droplets of cytoplasm, chloroplasts and mitochondria. The purified preparation was further homogenized and centrifuged, and contained only small droplets and a few mitochondria.

These data differ in several respects from those of Coombs and Baldry[4]. *Acetabularia* chloroplast preparations have unusual stability which may be due to the relatively impermeable outer membrane which prevents loss of photosynthate[1]. The ability of these chloroplast preparations to synthesize sucrose, their high rate of photosynthesis without lag phase, and their dark respiration, may be due in part to the retention of important enzymes, co-factors or intermediates by this membrane. The level of cytoplasmic contamination is low in these preparations, but some mitochondria are present[3]. The amount of such contamination can be varied experi-

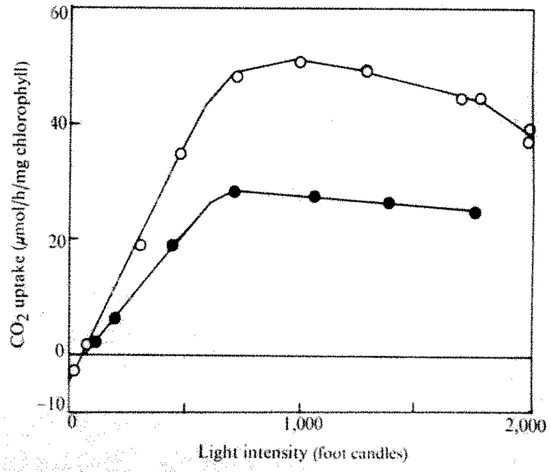

Fig. 3 The effect of light intensity on photosynthesis of chloroplasts in liquid medium (●) and the artificial leaf (○) at 500 p.p.m. CO_2.

mentally, however, and does not affect the entry of ^{14}C into major products of photosynthesis (Table 3). We therefore conclude that much of the photosynthesis metabolism under study is that of chloroplasts and not of the small amount of contaminants present. Purification reduces the rate of CO_2 fixation slightly, but it reduces the rate of dark respiration rather more (Table 3). Therefore the dark respiration may be attributable to cytoplasmic impurities.

The artificial leaf using an *Acetabularia* chloroplast preparation is a stable system, capable of normal photosynthesis. Because of its experimental convenience, and the similarity of its behaviour with that of chloroplast suspension and whole cells, it is potentially valuable for studying the intermediary metabolism and control mechanisms of photosynthesis and photorespiration.

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Transfer of Nitrogen-fixation Genes by Conjugation in *Klebsiella pneumoniae*

THE study of biological nitrogen fixation at the genetic level has been restricted by the lack of a suitable method of gene transfer in nitrogen-fixing bacteria. Mutants of *Azotobacter vinelandii*[1,2] and *Clostridium pasteurianum*[3] defective in nitrogen fixation have been isolated and characterized, but the transfer and mapping of the nitrogen fixation (*nif*) genes have not so far been possible.

The species *Klebsiella pneumoniae* includes strains which fix nitrogen if the environment is anaerobic. Matsumoto and Tazaki[4] have described fertile strains of *K. pneumoniae* which bring about gene transfer by conjugation and they have constructed a genetic linkage map of *K. pneumoniae*[5] which is similar to that of *Escherichia coli* and *Salmonella typhimurium*. We have found that these fertile *K. pneumoniae* strains do not fix nitrogen. Some of the transmissible bacterial plasmids which promote genetic recombination in other genera of the Enterobacteriaceae, however, are readily transferred to *Klebsiella* strains. Here we report the occurrence of chromosome transfer, mediated by a de-repressed R factor, in the nitrogen-fixing strain *K. pneumoniae* M5a1. We also report the transfer by conjugation of nitrogen-fixation genes from wild type *K. pneumoniae* to mutants defective in nitrogen fixation (nif^-) and present preliminary linkage data on some nitrogen fixation markers.

The strain used, *Klebsiella pneumoniae* M5a1, is a nitrogen-fixing organism originally isolated from a 2,3-butanediol fermentation[6]. It gave no transfer of chromosomal markers in matings with auxotrophic derivatives of *K. pneumoniae*, strain K1–8, provided by Dr H. Matsumoto, which is known to act as a recipient of genetic material[4]. However, chromosomal transfer was brought about in M5a1 by introducing a de-repressed I-type R factor, R144drd3, into this strain from its original host, *E. coli* J53. R144drd3 transferred chromosomal genes to auxotrophic M5a1 recipients at slightly lower recombination frequencies than those reported for this sex factor in F^- *E. coli* K12 (ref. 7) (Table 1). However, when M5a1 was mated with *E. coli* carrying the F-like R factor mutants R1drd19 to R1drd16, M5a1 clones were obtained which were characteristically drug-resistant, but which gave no transfer of drug resistance markers in matings with F^- *E. coli* K12 and were resistant to F-specific phage. In contrast, M5a1 carrying R144drd3 transferred drug resistance at high frequency to K12 and was sensitive to I-specific phage. It therefore seems likely that the drug resistance determinants of these two de-repressed F-like R factor mutants became segregated from the sex factor during transfer to M5a1. A similar phenomenon has been observed with R factor transfer in *Salmonella typhimurium*[8].

Table 1 Characteristics of *K. pneumoniae* M5a1 after Mating with *E. coli* Strains carrying De-repressed Mutant R Factors

De-repressed R factor	Drug resistances conferred	Chromosomal recombinants per donor cell for		Sensitivity to male specific phage	
		leu$^+$	*his*$^+$	μ_2	if_2
None	—	$< 10^{-9}$	$< 10^{-9}$	–	–
R144drd3	Km	2×10^{-5}	4×10^{-5}	–	+
R1drd16	Km Cm Ap Sm Su	$< 10^{-9}$	$< 10^{-9}$	–	–
R1drd19	Km Cm Ap Sm Su	$< 10^{-9}$	$< 10^{-9}$	–	–

E. coli strains carrying the de-repressed mutant R factors were mated with *K. pneumoniae* M5a1, drug-resistant recipient M5a1 clones were purified and mated with auxotrophic streptomycin-resistant derivatives of M5a1. One volume of donor culture grown to log phase in broth (2 to 5×10^{-8} organisms/ml.) was added to 9 volumes of recipient culture and incubated for 4 h at 37° C without shaking. The bacteria were then centrifuged, resuspended in buffer and plated at various dilutions on selective media to determine the number of recombinants and the number of donor cells present. Streptomycin was used to counter-select the donor at 250 µg/ml., or 2 mg/ml. where the R factor carried a determinant for streptomycin resistance. Phage sensitivities were measured by spotting phage on to semi-solid nutrient agar overlays containing the bacteria under test. + Indicates visible lysis.

To study the transfer of nitrogen fixation markers, a series of mutants of *K. pneumoniae* M5a1, defective in nitrogen fixation (nif^-), were isolated as follows. A streptomycin-resistant derivative of M5a1 was mutagenized with 20 mM isopropylmethane sulphonate for 1 h at 37° C, washed by centrifugation to remove the mutagen and then grown in air overnight in nutrient broth to allow segregation of mutant phenotypes. The mutated culture was then washed by centrifugation to remove fixed nitrogen and was sparged with N_2 for 18 h at 34° C to allow induction or de-repression of nitrogenase. Penicillin (16,000 IU/ml.) and D-cycloserine (1 mg/ml.) were then added and the culture was sparged with N_2 for a further 6 h to enrich nif^- mutants. Surviving bacteria were collected on a membrane filter and washed free of the antibiotics before further growth in nutrient broth. After several such antibiotic enrichments, nif^- mutants were sought by plating anaerobically under N_2 on minimal medium containing low nitrogen as 10 µg NH_4Cl-N/ml. Presumptive nif^- mutants were small and colourless on this medium whereas the wild type produced large colonies which were distinctly yellow. The acetylene-reducing activity of the presumptive nif^- isolates was almost negligible compared with wild type (Table 2), indicating that these mutants are defective in nitrogen fixation. Full details of the biochemical properties of these mutants will be published later.

Table 2 Comparison of Acetylene Reduction in Wild Type, *nif*$^-$ Mutants and *nif*$^+$ Recombinants of *K. pneumoniae* M5a1

Strain	nmol ethylene formed/min/mg dry weight
Wild type	20.7
nif 12	0.3
nif 2	<0.1
nif 3	<0.1
nif 9	<0.1
nif$^+$ 3 recombinant	18.1
nif$^+$ 9 recombinant	17.4

The bacteria were grown in a modified Hino and Wilson's N-free medium[10] supplemented with 1 mg of yeast extract/ml. in "medical flat" flasks sparged with N_2 at 30° C. Samples of 2 ml. were removed from the culture and tested for acetylene reduction under argon at 30° C in sealed 25 ml. flasks containing 1 ml. of acetylene which were shaken slowly.

Crosses were performed between *K. pneumoniae* M5a1 carrying R144drd3 and *nif*$^-$ mutants of M5a1. *Nif*$^+$ recombinants were selected for anaerobically on nitrogen-free minimal medium. The donor was counter-selected with streptomycin; the concentration, 5 mg/ml., was high because this antibiotic is far less effective in anaerobic conditions. In typical crosses, nitrogen-fixing recombinant colonies appeared at a frequency of approximately 10^{-5} per donor organism. Recombinant colonies after purification on nitrogen-free minimal medium gave acetylene-reducing activity equivalent to the wild type (Table 2).

We have also transferred an unidentified sex factor, from Matsumoto's *Klebsiella* strain D8, to M5a1 and obtained a fertile M5a1 strain which transferred genetic information, including *nif*, to M5a1 recipients. The recombination frequencies, however, were very low and the system was not studied further.

While this work was in progress, Streicher, Gurney and Valentine[9] reported the transduction of the nitrogen fixation genes in *K. pneumoniae* M5a1 using bacteriophage P1 and showed that several *nif* genes were located near the histidine operon on the linkage map of *K. pneumoniae*; we acknowledge advance information on their findings from Dr R. Valentine. Their observations prompted us to consider the relationship of the *his* and *nif* loci. Crosses were performed between M5a1 (R144drd3) and multiple auxotrophic *nif*$^-$ mutants of M5a1, the recombinants were purified on selective media and then scored for inheritance of *nif*. We find that *his* shows a 95% linkage to *nif* 9 and an 85% linkage to *nif* 2, thus confirming that *his* and *nif* are closely linked.

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Metabolism of Δ^9-Tetrahydrocannabinol by Lung and Liver Homogenates of Rats treated with Methylcholanthrene

Δ^9-TETRAHYDROCANNABINOL (Δ^9-THC) is metabolized *in vitro* by the postmitochondrial supernatant of rabbit liver to yield 11-hydro-Δ^9-THC[1], said to be as pharmacologically active as Δ^9-THC itself[2,3], while at least two other metabolites have been detected[2]. Because psychoactive cannabinoids are effective in cannabis smoking, we have studied the transformation of Δ^9-THC by the postmitochondrial supernatant of the rat lung and we have compared the chromatographic properties of the Δ^9-THC metabolites which were produced *in vitro* by the postmitochondrial supernatant of liver and lung from untreated rats and from rats pretreated with 3-methylcholanthrene[4].

Young male Sprague–Dawley rats (Zivic Miller, Pittsburgh, 50–60 g) were injected intraperitoneally with 3-methylcholanthrene (20 mg/kg) in 0.25 ml. of sesame oil daily for 4 days. Control rats were given injections of sesame oil. Each group consisted of three rats, fed liberally with Purina chow. The rats were decapitated, the livers were quickly removed, chilled in an ice bath and homogenized with five volumes of 0.25 M sucrose, while the lungs were homogenized with ten volumes of the same sucrose solution. The homogenates were centrifuged at 9,000*g* for 20 min at 0°–5° C and the subsequent postmitochondrial supernatant was used as the enzyme source. The reaction mixture contained, in a total volume of 0.50 ml., 17.7 nmol Δ^9-THC-^{14}C (12,500 d.p.m./nmol), 1 µmol glucose 6-phosphate, 100 nmol NADP, 100 nmol nicotinamide, 1 µmol $MgCl_2$, 1 U glucose 6-phosphate dehydrogenase, 30 µmol Tris-HCl (*p*H 7.4) and 0.03 ml. (0.45 mg protein) of the postmitochondrial supernatant in the case of liver, or 0.20 ml. (1 mg protein) in the case of lung. (Δ^9-THC-^{14}C, which was synthesized by Research Triangle Institute, North Carolina, is labelled on the 2- and 4-positions of the benzene ring; its specific activity is 5.5 mCi/nmol.) The mixture was incubated for 15 min at 37° C and the reaction was stopped by shaking vigorously with 10 ml. of petroleum ether and 2.0 ml. of distilled water for 5 min in a separating funnel. The cannabinoids in the aqueous phase were then removed with ethylacetate. These two organic phases extract the radioactivity almost completely. After evaporation to dryness the radioactive compounds were dissolved with a small amount of dehydrated ethanol and applied on thin-layer plates with silica gel G. Δ^9-THC and its metabolites were chromatographed twice, with a solvent system of cyclohexane–diethyl ether (4 : 1) followed by another solvent system of chloroform–cyclohexane–acetic acid (50 : 40 : 10). The spots of nonradioactive compounds were detected by spraying the plate with 0.2% O-dianisidine tetrazolium chloride (fast blue salt B) in 2 M NaOH[5]; the radioactive spots could be detected by autoradiography. The radioactivity of the absorbent scraped from the plates was determined by liquid scintillation counting. Protein was determined by the method of Lowry *et al.*[6].

Δ^9-THC-^{14}C was incubated with the postmitochondrial supernatant of lung and liver in the conditions described. When an aliquot of the reaction was extracted and chromatographed on the thin-layer plate, several radioactive products as well as Δ^9-THC-^{14}C could be detected (Fig. 1). Co-chromatography with authentic samples of Δ^9-THC, Δ^8-THC and 11-hydroxy-Δ^8-THC corroborated that Δ^8-THC could not be distinguished from Δ^9-THC by this method and that the R_F of 11-hydroxy-Δ^8-THC was 0.30. This result suggests that the radioactive metabolite with an R_F of 0.30 may be 11-hydroxy-Δ^9-THC.

We compared the enzymatic production of several radioactive metabolites from Δ^9-THC, by lung and liver of untreated rats and rats receiving 3-methylcholanthrene. The results are summarized in Table 1. The enzymes of the postmitochondrial supernatant of rat lung could produce several metabolites of

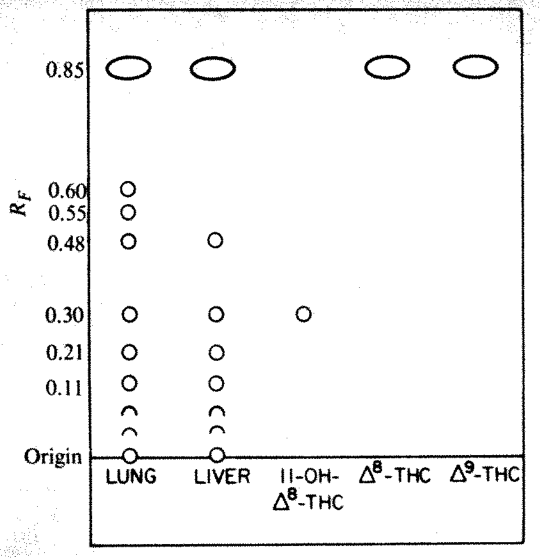

Fig. 1 Separation of Δ^9-THC and its metabolites by thin-layer chromatography.

Δ^9-THC. Moreover, by the pretreatment with 3-methylcholanthrene the metabolism of Δ^9-THC was stimulated in the lung but not in the liver. In the liver, however, the enzyme activity responsible for the formation of compounds with R_F values of 0.30 and 0.48 was induced by 3-methylcholanthrene.

The compounds of R_F 0.60 and 0.55 were produced by the postmitochondrial supernatant of the lung, but they could not be detected when Δ^9-THC was incubated with the liver homogenates. The compounds of R_F 0.48 were formed to a greater extent by lung supernatant than by liver supernatant. On the other hand, the enzymatic formations of the compounds with R_F 0.30 and 0.21 were more conspicuous in the liver than in the lung.

Generally, the liver is considered to be the principal site for the transformation of several drugs, but nonhepatic tissues such as the lung and the kidney can metabolize various drugs[4,7-10]; on the basis of histochemical findings, for example, Wattenberg *et al.*[10] reported that the alveolar walls of rat lung might be the metabolic site for 3,4-benzpyrene production. Our results show that Δ^9-THC is also enzymatically converted by rat lung, but that the pathways of Δ^9-THC metabolism in lung homogenates might be different from those detected in liver.

Ho *et al.*[11] administered Δ^9-THC-^{3}H by smoking and found that cannabinoids are retained by lung and that in this tissue, the radioactivity remains higher than in all other tissues for longer than 24 h. Moreover, the level of radioactivity in brain and liver is lower than that of lung for up to 7 days. This observation suggests that when Δ^9-THC is administered by smoking, the lung may be more important than the liver for the storage and biotransformation of Δ^9-THC. We found that treatment with 3-methylcholanthrene induced the enzyme system responsible for the metabolism of Δ^9-THC in the lung but had no effect on that in the liver. In the lung of rats receiving 3-methylcholanthrene the rate of Δ^9-THC metabolism is equal to that in liver, suggesting that in these animals the lung plays a critical role in the biotransformation of Δ^9-THC. We also found that liver homogenates of rats receiving phenobarbital (75 mg/kg) for 4 days metabolized Δ^9-THC at a rate twice that of liver homogenates from untreated rats. The induction of lung but not of liver enzymes for Δ^9-THC metabolism by polycyclic hydrocarbons may be consistent with a suggestion made by Mannering *et al.*[12] that a microsomal haemoprotein different from the so called P-450 is formed in the liver when 3-methylcholanthrene is administered. Possibly the enzyme system responsible for the metabolism of Δ^9-THC in the lung recognizes a microsomal haemoprotein different from P-450, and this property may explain the selective induction of Δ^9-THC metabolism by 3-methylcholanthrene in the lung. The precise mechanism of this selective induction by polycyclic hydrocarbons and the pharmacological implications of the different biotransformation of Δ^9-THC in lung and liver is under investigation in our laboratory.

Table 1 Effect of Methylcholanthrene on the Metabolism of Δ^9-THC in Rat Lung and Liver

Metabolite	Radioactive metabolites formed (pmol/min/mg protein) ± s.d.			
	Lung		Liver	
	Control	3-MC*	Control	3-MC*
R_F 0.60	30.4 ± 4.1	42.4 ± 2.3	0	0
R_F 0.55	29.6 ± 1.2	45.4 ± 4.0	0	0
R_F 0.48	23.8 ± 2.5	78.1 ± 2.4	9.8 ± 2.9	27.3 ± 2.6
R_F 0.30†	9.4 ± 5.0	15.6 ± 10.3	32.1 ± 15.5	94.6 ± 23.6
R_F 0.21	12.0 ± 3.1	19.8 ± 4.5	206.3 ± 53.0	120.1 ± 39.6
R_F 0.11	7.0 ± 5.0	19.1 ± 7.4	20.4 ± 5.5	33.0 ± 3.5
Total rate‡ of Δ^9-THC metabolism	172.8 ± 18.1	406.2 ± 36.8	358.5 ± 77.7	384.8 ± 102.7

* Injected intraperitoneally with 20 mg/kg of 3-methylcholanthrene.
† This compound may be 11-hydroxy-Δ^9-THC.
‡ This value indicates the amount of metabolized Δ^9-THC.

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Fluid Friction of Fish Slimes

WHEN dissolved in water, the natural slimes of most of the fishes we have tested have a remarkable capacity to decrease greatly the friction of water when flowing in the turbulent state. In one species, a dilute solution of its slime was found to reduce the friction of water by as much as 65.9%; reductions of 57% to 63% were frequently obtained with the slimes of other species. These measurements have led us to the view that the slimes of many (but not all) fishes assist in locomotion by reducing the drag or resistance which water offers to their bodies.

Slime samples were taken from the live fishes immediately after removal from the water and after excess water had been drained off their bodies. The slime was diluted to various concentrations with clean water from the natural environment and then tested in a portable rheometer.

The rheometer works on a principle described by Hoyt[2]. A glass plunger (Fig. 1) drives the solution upwards through a stainless steel tube 6 inches long and 0.023 inch internal diameter. At two points, 3 inches apart, the tube is pierced with a side outlet, and the static pressure of the moving fluid at these two locations is sensed by electrical transducers and read directly on two meters. The rheometer was first calibrated using plain water.

In most cases, the pressure decrease measured with fish slime solution was substantially lower than that measured with plain water, and the corresponding reduction of friction can be calculated from the ratio of the two differences of pressure. The fluid velocity reached 45 feet per second, corresponding to a pipe Reynolds number of nearly 8,000, which in turn implies that the flow in the tube is well within the turbulent regime for water.

The results are shown in Fig. 2 for saltwater species and in Fig. 3 for freshwater species; and the slime of the Pacific barracuda, *Sphyraena argentea*, is the most effective reducer of friction of all the fish tested, with a maximum reduction of 65.9% when the natural slime is at 5% concentration. With more concentrated solutions, the friction reduction diminished slightly. The barracuda curve represents data taken from eleven individual fish all of the same species, 26–31 inches long, and caught on different days. The barracuda curve rises steeply for very low slime concentrations. A 44% friction reduction was obtained with a solution of only 3/4 of 1% barracuda slime (Fig. 4).

The results of the work with the slimes of halibut, *Paralichthys californicus*, and other sea species are also shown in Fig. 2. Halibut slime is almost as good a friction reducer as that of barracuda. The curves for most of the other species of saltwater and freshwater fishes shown are similar but do not rise as steeply as those of halibut and barracuda.

The measurements on California bonito, *Sarda chiliensis*, were a surprising exception. This slime seems to be almost ineffective as a reducer of water friction. Tests on specimens caught on different days gave consistent data, verifying ineffectiveness of this slime. Two sea animals that are not fishes have been included for comparison; the mollusc known as the nut brown cowry, *Cypraea* (*Zonaria*) *spadicea*, and the California hagfish whose slime was measured by J. Hoyt and W. White (personal communication). The maximum friction reduction obtained for each species is given as well as values of friction for low concentration solutions. The latter is important, for a slime which gives a large friction reduction at relatively low concentration in water is considered very effective. If slime is added to still water, it typically stays separate from it; we have called this property "reluctance". Most of the slimes, though not all, dissolve in water when stirred or agitated.

On the whole, the slimes of fishes seem to possess frictional properties which are adapted to the need of the species for speed, or to its life habits and activities. The barracuda, which had the most effective slime tested, is a streamlined predator (Fig. 4). The closely related species, *Sphyraena*

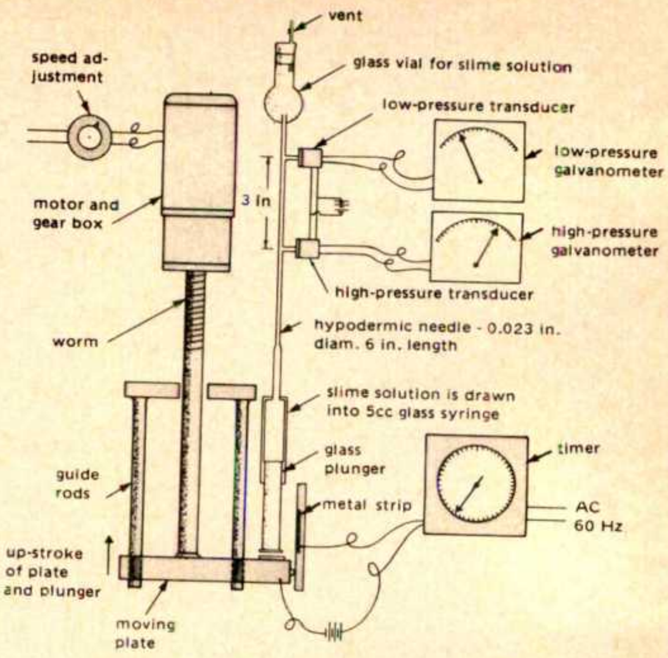
vent
speed adjustment
glass vial for slime solution
low-pressure transducer
low-pressure galvanometer
motor and gear box
3 in
high-pressure galvanometer
high-pressure transducer
worm
hypodermic needle - 0.023 in. diam. 6 in. length
slime solution is drawn into 5cc glass syringe
glass plunger
timer
guide rods
metal strip
AC 60 Hz
up-stroke of plate and plunger
moving plate

Fig. 1 Schematic diagram of rheometer.

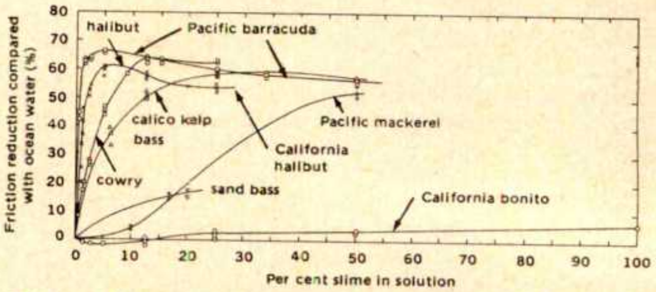

Fig. 2 Friction reduction of slimes of seawater fish when dissolved in ocean water in various concentrations.

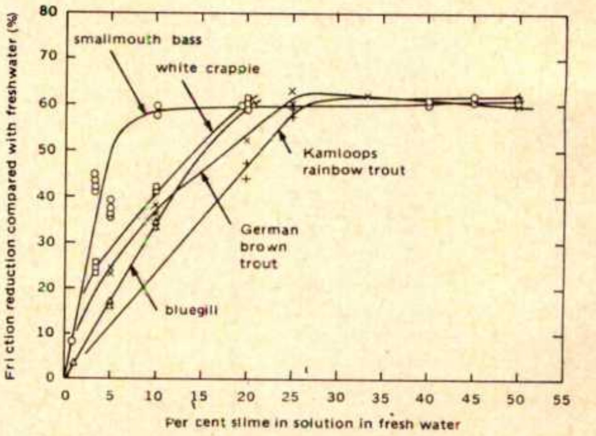

Fig. 3 Friction reduction of slimes of freshwater fish when dissolved in freshwater in various concentrations.

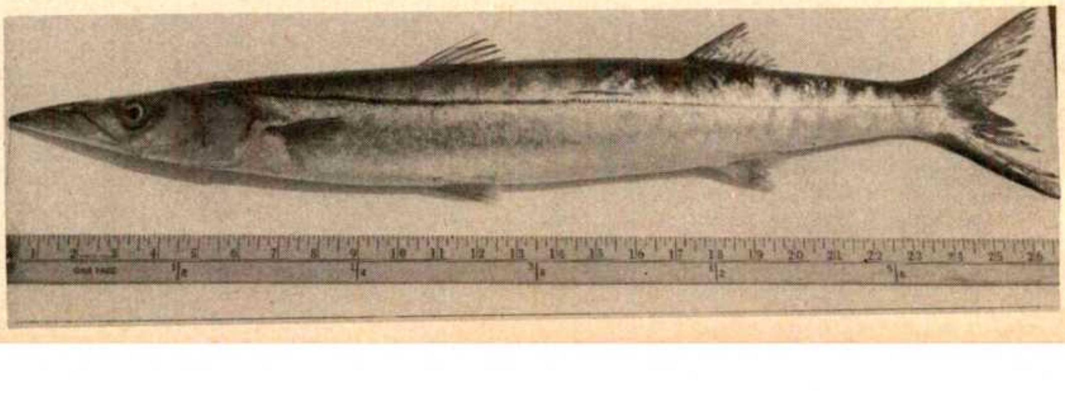

Fig. 4 Pacific barracuda.

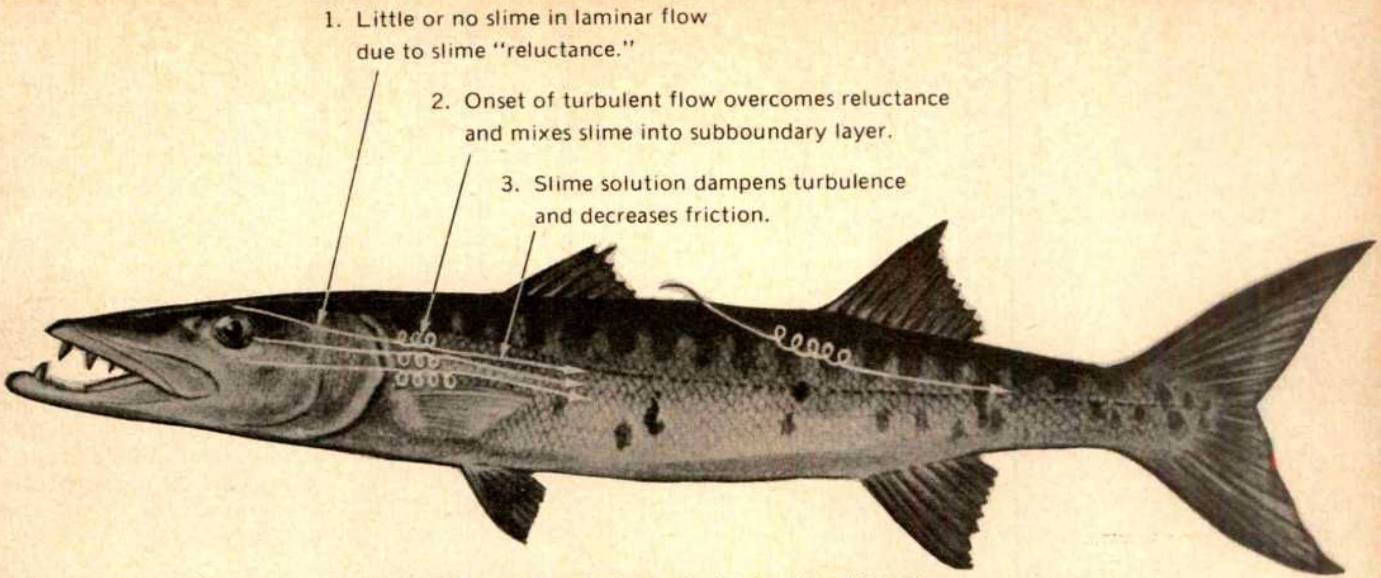
1. Little or no slime in laminar flow due to slime "reluctance."
2. Onset of turbulent flow overcomes reluctance and mixes slime into subboundary layer.
3. Slime solution dampens turbulence and decreases friction.

Fig. 5 Rosen–Cornford hypothesis of action of fish slime.

barracuda, has been measured by D. Gero[3] to swim at 27.3 miles/h, which is very fast for an aquatic animal. The halibut, which also has effective slime, catches fish by means of long, swift lunges.

The trouts are reasonably swift swimmers, and the slimes of the adults are correspondingly fairly effective. On the other hand, the California hagfish has no need for speed, being a parasite and scavenger. Its slime, although thick and profuse, is a poor reducer of water friction. The slime of this animal could not be dissolved except by forcibly homogenizing it with water in a mechanical blender. Similarly, the white croaker, which feeds on slow sea life and has little need for speed, has a thick curdy slime, insoluble in seawater, and which could not be put through the rheometer. Two exceptions are the slimes of the Pacific mackerel, *Scomber japonicus*, and the California bonito, both of which are fast swimmers. The mackerel's slime becomes effective only at a concentration of 50% slime, 50% water; and that of the bonito produces no more than 6.4% friction reduction at 100% concentration. Perhaps this fish attains its propulsive speed in other ways, possibly by the formation of a large organized vortex system at its sides, similar to the remarkable fish vortex system discovered by Rosen[4]. The slime of the nut brown cowry was quite effective as a friction reducer. Although this animal has no need for speed, its slime provides good lubrication between its tissues and its hard shell as it moves about.

The amount of solid substance in the slime of the small mouth bass, *Micropterus dolomieui*, was measured by weighing the residue left after the water had evaporated under a vacuum at room temperature. We found that the natural slime as taken from the fish consists of only 0.153% solids by weight, and possibly half of this is water of crystallization. With an assumption that barracuda slime would contain about the same percentage of solids, and taking the measurement that a 1.5% barracuda slime solution produced a friction reduction of 62.9%, we compute:

$$\frac{0.153}{100} \times 0.5 \times \frac{1.5}{100} = 0.0000115$$

This means that the barracuda may need to supply only about 11.5 parts of its own organic solid substances to every million parts of water flowing in the boundary layer over its body in order to decrease water friction by 62.9%. Similarly, this fish, with a 3/4 of 1% solution, need supply only 5.7 p.p.m. of its organic solid substances to decrease water friction by 44%.

We propose the following hypothesis (Fig. 5). Most of the time, fishes swim quite slowly and the sub-layers of water very close to the body may not be turbulent. The "reluctance" of the slime prevents the loss of the slime coat. But during the short periods when the fish must swim rapidly to catch its prey, or to escape danger, the sub-layers of water break into turbulent flow and the reluctance of the slime is overcome, so that a small amount goes into solution. The turbulence at that point automatically produces its own suppression, for the dilute slime solution it has created dampens further turbulence and flows with lower friction over the scales. As the fish swims more rapidly its body is enveloped by a thin boundary layer of this extremely dilute slime solution which suppresses any turbulence and substantially lowers the water friction on the body. Thus with only a minute expenditure of organic solid substances to make the necessary quantity of slime solution, the fish can attain a considerably higher speed than would otherwise be possible.

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Anoxia in Mosquito Pupae under Insoluble Monolayers

The dependence of mosquito larvae and pupae on the air–water interface for respiration suggests several opportunities for insect control. The use of soluble surfactants to vary the surface tension[1–3] is reported to have been effective but the substances employed would not be used on water intended for drinking or irrigation. Insoluble monomolecular layers of lauryl alcohol have also been reported[4] to be effective against pupae of *C. pipiens quinquefasciatus*. We now describe the effect of several monomolecular films on mosquito pupae of several species.

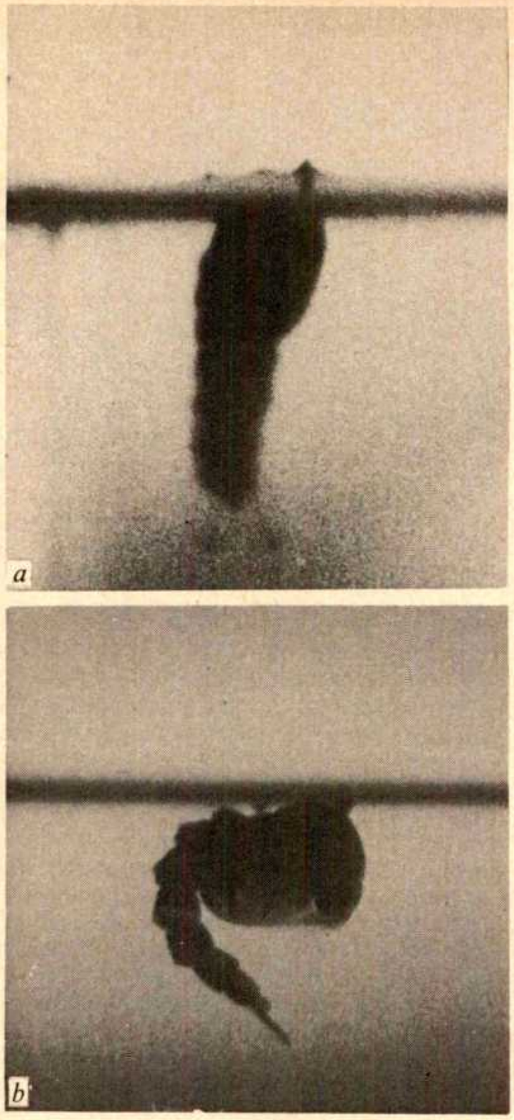

Fig. 1 *a*, An energetic but unsuccessful attempt by a mosquito pupa to penetrate a monolayer of lipid (from a high speed cine sequence taken at 240 frames/s). *b*, Mosquito pupa in the normal respiring position.

The study described here began with the observation that a monolayer of crude lipid extract was 100% lethal to pupae of *Anopheles* (*Cellia*) *stephensi* Liston, and to pupae of *Aedes* (*Stegomyia*) *aegypti* (Linnaeus) in the underlying water. The method has since proved equally successful with all other species investigated, for example, *An. albimanus*, *An. atroparvus*, *An. gambiae*, *An. quadrimaculatus*, *An. phaeroensis* and *Culex fatigans*. For comparison, the effect of other insoluble monolayers having a range of maximum equilibrium spreading pressures (π_e) was determined at a constant temperature of 27° C. Surface pressures were measured by the pull on a thin glass slide supported in the interface by a sensitive electrobalance. The vessel, containing about forty pupae in distilled water, was temperature equilibrated; the water surface was cleaned to constant tension by suction and this reading on the balance was taken as zero pressure. The film was spread and the maximum pressure noted. The number of successful adult emergences, the number of adults trapped by surface tension forces at the interface, and the number of pupal deaths were recorded. Table 1 presents the results obtained using *Ae. aegypti*.

The results clearly indicate a critical pressure of approximately 45 dynes/cm, beyond which 100% mortality occurs in the pupal stage. Below this surface pressure a percentage of the emergent adults fails to get off the surface and dies. The total mortality therefore remains high even if the film is incompletely spread and consequently not exacting its full pressure. The mechanism responsible for adult mortality is seemingly a "wetting process" which causes submergence of the legs and a general loss of flotation. This is observed readily by viewing the undersurface of the film. Evidence from high speed cine photographs[5] indicated that the lipid monolayer was behaving more like an elastic membrane at full pressure, thus preventing any penetration by the respiratory trumpet of the pupa. Pupae at the film surface exhibit characteristic patterns of movement which include energetic attempts to force one pupal trumpet through the film by sideways-orientated circular movements and frequent efforts apparently to dislodge the film with the tail (Fig. 1*a*). Death occurs after 2–3 h, but before this the pupae sink to the bottom of the container and are unable to reach the surface; they exhibit violent flexing movements of the body and tail, probably due to a build up of lactic acid and other anaerobic metabolites in the muscles. Identical behaviour and a similar pattern of death were observed when a glass plate was placed on a normal water surface to exclude all air.

Table 1 Effect of a Range of Insoluble Monolayers on Mortality of *Aedes aegypti* Adults and Pupae

Film substance	π_e dynes/cm	Percentage of total kill as: Adults	Pupae
None	0	0	0
Lysophosphatidyl ethanolamine	24.9	0	0
Methyl palmitate	28.0	0	0
Oleic acid	32.0	0	0
Cetyl alcohol	34.6	0	0
Cholesterol	38.0	35.0	0
Phosphatidyl serine	41.4	32.5	0
Lauryl alcohol	43.2	40.0	0
Dog brain lipid	45.7	0	100
Egg lipid	47.9	0	100
Egg lecithin	49.0	0	100
Glass plate	—	0	100

Attempts to asphyxiate larvae by the same methods were relatively unsuccessful, probably because of the different structure of the small larval spiracle which easily penetrated films of even the highest surface pressure. Other workers, however, have reported[4] that larvae are killed under lauryl alcohol films.

Bio-degradable, non-toxic (edible) lipids, spread at the surface saturation concentration of about half an ounce per acre of water, afford a potentially valuable method of mosquito control. Such films are insoluble in water, do not prevent gaseous exchange across the air–water interface and are therefore in no sense destructive of aquatic (fish or plant) life. Because the films are a physical rather than a chemical "block" to pupal development it seems less likely that genetically resistant strains will arise. Effective methods of application in the field (particularly on ricefields and in water storage containers), including automated procedures, are to be investigated.

We thank D. Sainsbury for assistance with the surface pressure measurements, the CDE Film Unit for preparation of the movie sequences, and J. G. Broadfoot for larvae and pupae.

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BOOK REVIEWS

Threats to the Reef

The Struggle for the Great Barrier Reef. By Patricia Clare. Pp. 224+15 plates. (Collins: London and Sydney, September 1971.) £2.50.

THE Great Barrier Reef of Australia is a vast complex of coral reefs which extend in length for more than 1,200 miles and occupy widths ranging from 16 to 200 miles off the coast of Queensland. Nobody who has spent more than a year upon it over 40 years ago, as I did, could have dreamt of its ever being endangered or that the question of its conservation could emerge as a major political issue.

But this is certainly what has happened and the sequence of events leading to this is well presented in this book by Patricia Clare. Disregarding a few purple patches, the reader will find a very clearly written story. Although there is no doubt where the author's sympathies lie, she has visited and interviewed widely and judiciously and presents both sides of the argument. This book is first-rate journalism; too good, incidentally, not to have an index.

Relevant additional reading for readers who are particularly interested in the subject, and which is not specifically mentioned in this book, are two articles by Dr D. W. Connell, president of the Queensland Littoral Society (*Biological Conservation*, **3**, 60; 1970; and 249; 1971), and a booklet, *The Future of the Great Barrier Reef*, which consists of a series of contributions presented at a symposium conducted by the Australian Conservation Foundation in the University of Sydney in May 1969.

Dangers facing the reefs are manifold—industrial and agricultural pollution, tourism, mining for coral rock and, most sinister, now also oil prospecting. Tourism is an insidious influence; a gradual spread of often tasteless and wasteful exploitation which largely affects inner and southern reefs but now reaches out to a most northern and offshore base at Lizard Island, a high rocky island within sight of the outermost ribbon reefs and only a little south of Cook's Passage.

Such invasion, which equally affects remote Pacific islands, is unlikely to be stopped, but at least some moderation should be imposed on the indiscriminate collecting of shells and corals, of sport fishing and of underwater spear fishing. These spectacular invertebrates and fishes are often hunted to near extinction. One theory as to the cause of the plague of crown-of-thorns starfish which are destroying reef corals over widely scattered areas in the Pacific attributes it to the collection of the large trumpet shell, *Charonia tritonis*, which preys on these starfish. But the more universal effect of pollutants, notably pesticides, has also been introduced as the chief cause of an underlying ecological imbalance.

Certainly the population explosion of this starfish first drew public attention to dangers affecting the Barrier Reefs, but confrontation came in 1967 when conservation interests, stimulated, as Patricia Clare describes, by action of the devoted few, proved great enough, when backed with soundly based argument, to ensure the rejection in the mining warden's court of an application to mine Ellison Reef for limestone. And this decision was made in spite of the urgent need for lime on the sugar cane fields of North Queensland. The effects of bauxite processing and of open cast mining for coal around Gladstone nevertheless become increasingly apparent.

With the later prospect of oil drilling, both State and Commonwealth Governments come into the picture. A report by Dr Harry Ladd, a most distinguished American reef geologist, approved exploitation under appropriate controls. Early last year, with the scene set for the operation of the oil-rig Navigator, the trade unions took action by threatening a ban on all goods and services. Clash of opinion between State and Commonwealth was resolved by the then Prime Minister, Mr Gorton, who stated that "In my view the slightest danger is too much danger" (a sentence that will surely endear him to all conservationists) and a Royal Commission, now sitting in Brisbane, was set up. The commission is unlikely to report before late in 1972.

This action by the Australian Government can be regarded as a triumph for conservation. Time is probably on that side but the real danger is lack of precise biological knowledge about coral reefs. What some of us began on the Barrier in 1928–29 has, for lack of public interest and money, had little addition. Only the Japanese, at their biological station at Koror in the Palau Isles, took biological studies somewhat further but their laboratory was destroyed in the war. There are now prospects of a Marine Research Institute to be built by the Commonwealth Government at Townsville in close proximity to the vigorous new James Cook University of North Queensland.

There is likelihood too of greater coordination of wider coral reef studies under the auspices of the Pacific Science Association. But knowledge in this field is painfully slow in coming. All interested in conservation generally and in coral reefs in particular must applaud those few Australians whose efforts, so well related in this book, have stimulated the growth of public concern in the conservation of the Great Barrier Reef and so in the study of its richly varied ecosystems.

C. M. YONGE

Thermogenesis

Nonshivering Thermogenesis. (Proceedings of the Symposium held in Prague, April 1–2, 1970.) Edited by L. Jansky. Pp. 310. (Academia: Prague, 1971.) (Distributed by Butterworths, London.)

THERE is much justification for the popular and cynical view on symposium proceedings that if the contributions are worthy of note they either have been or will be published elsewhere. Thus library and laboratory shelves are cluttered with the neglected literary remnants of scientific symposia. However, it would be a great pity if this particular series of review and research papers by a small group of internationally acknowledged leaders in the field of thermoregulatory thermogenesis were to suffer such treatment.

That heat production in response to cold stress may not always involve the contractile activity of muscles was first proposed by Claude Bernard in 1876, but convincing demonstrations of the phenomenon were reported only ten to twenty years ago. The subsequent quest for the sites and the nature of nonshivering thermogenesis was enlivened, but certainly not resolved, by R. Em. Smith's discovery in 1960 of a special role of brown adipose tissue in the nonshivering thermogenesis of the white rat. Only those researchers directly and intimately involved in the study of cold-induced thermogenesis can be thoroughly conversant with the now vast literature pertaining to this complex and controversial subject. For those of us who are outside this immediate field it has become increasingly difficult to maintain a balanced appraisal of the accumulating evidence. It involves the contribution of different tissues in nonshivering thermogenesis: the relative importance of shivering and nonshivering thermogenesis in different species and in different circumstances; the changes in the balance between the contributions of shivering and nonshivering thermogenic processes during postnatal development and during acclimatization to cold stress; the role of nonshivering thermogenesis during arousal from hibernation and other forms of torpor; the neuronal and hormonal control of shivering thermogenesis; and the biochemistry of nonshivering thermogenesis.

The assembly of this small group of experts in Prague last year has resulted in the publication of a comprehensive, authoritative and eminently readable series of essays that can be confidently recommended to anyone who needs a relatively painless introduction, or reintroduction, to this exciting field of study.

Although, generally speaking, verbatim reports of the discussions which follow contributions to colloquia are of little value, in this instance I have found the discussions well worth attention. Subsequent reference to this volume will be hampered by the absence of an index. The English is not quite impeccable, but as one who cannot read with confidence in other languages I have nothing but praise for the high standard of Dr Jansky's editorial efforts as well as for his own important contributions to the study of nonshivering thermogenesis.

JOHN BLIGH

Mature Fruit

The Biochemistry of Fruits and their Products. Vol. 1. Edited by A. C. Hulme. (Food Science and Technology: a Series of Monographs.) Pp. xviii+620. (Academic: London and New York, November 1970.) £10; $30.

As part of a series on food science and technology, the editor quite properly warns that in this book the term " fruit " is to be used in the strictly commercial sense and that, even so, only those fruits most important from an economic standpoint have been chosen. The less-specialized reader will be encouraged to know that in this first, general volume, the contributors have been allowed to step outside this limit if required by their theme; even *Rosa* appears here and there.

Again, although the primary study is to be of the maturation, post-harvest physiology, senescence and storage of fruits rather than of their growth processes, a short section on growth and pre-harvest factors is provided. It was indeed here that I found a chapter which seemed to me to be of outstanding merit —" The Physiology and Nutrition of Developing Fruits " by E. G. Bollard. This writer describes, in terms ranging from molecular to morphological, how mature fruits achieve this status, and also their relationship with the parent plant. The reader may profitably begin with this section.

It will already have become obvious that, fortunately, Dr Hulme believes that fruit biochemistry and physiology "cannot usefully be separated". Nor should they be bereft of a background in intracellular and higher levels of structure. One hopes that these latter will find a place in the second volume, which is to present the biochemistry and physiology of individual fruits or types of fruit, and also the biochemistry of fruit processing.

This volume makes a classical approach though the constituents of fruits, with chapters on sugars; hexosans, pentosans and gums; pectic substances; organic acids; amino-acids; proteins; enzymes; lipids; volatile compounds; fruit phenolics; carotenoids and triterpenoids, and vitamins. Then comes the section on growth and pre-harvest factors, including hormonal factors, followed by the ethylene factor, the climacteric and ripening. The book ends with a brief consideration of the physiological disorders of fruits.

There are some shortcomings; for example, although chemical constituents are well covered in the subject index, it is less complete in other respects, and when the number of structural formulae in a chapter exceeds seventy the use of Roman numerals is cumbersome. But in general the editor and contributors are to be congratulated. Rarely may the old phrase of " filling a long felt need " be aptly applied: it is well and efficiently earned in this case.

G. A. D. JACKSON

A Big-bang Universe?

Modern Cosmology. By D. W. Sciama. Pp. viii+212+18 plates. (Cambridge University: London, September 1971.) £3.60; $8.95.

THIS is a survey of the modern developments in cosmology, intended, according to the author, for "readers with only a modest knowledge of mathematics and physics". It is well illustrated with diagrams and photographs and makes interesting reading even for an expert in the field.

The book is divided into sixteen chapters with a theoretical chapter at about the half-way stage on the models of the universe. For the benefit of the non-specialist the first five chapters provide a general description of stars, the Milky-Way system, the external galaxies, radio sources and the quasistellar objects. The associated astrophysical processes such as thermonuclear reactions, cosmic rays, X-rays and γ-rays, neutrinos, gravitational waves, magnetic fields are also briefly described. The next two chapters discuss the observational data on the distribution of radio galaxies and the quasistellar objects. Then comes the theoretical discussion of the simplest cosmological models. For simplicity there is a brief mathematical discussion which is based on the Newtonian laws of gravitation and motion, in spite of their limited validity. The results from the less ambiguous but more complex theory of relativity are then quoted—and in many ways they are similar to the Newtonian results. With these models in mind the author looks at further astronomical data in the following eight chapters. This largely includes evidence (or lack of it) for the intergalactic matter, the abundance of elements (in particular the helium–hydrogen ratio) and the observed microwave background. The discussion throughout the book is fairly wide but is not deep enough to satisfy the more curious reader. If he wants further information he must look to the more technical reviews available or to the original articles. But, alas, this book does not give references to guide such a reader!

A typical reader is most likely to come to the following conclusions: (1), the redshifts of the quasistellar objects are of cosmological origin; (2), the microwave background is of primaeval (big-bang) origin; and (3), the steady state universe is ruled out by the observations. To what extent are these conclusions justified? One may recall Burbidge's recent remark "that views in cosmology at any epoch are largely determined by the ideas of a few strong individuals, rather than by an objective appraisal of the information available" (*Nature*, **233**, 36; 1971). Cosmology has come a long way since Hubble observed the redshift from distant galaxies. As this book shows, the observational astronomer has invented numerous ingenious ways of probing the universe. But the environment has limited the precision of his observations when compared with the precision obtained by a laboratory scientist. This in turn has led to ambiguity of interpretation and to numerous controversies. Cosmology, however, thrives on such controversies; for instance, the three statements given earlier are still subjects of controversy, and should not be taken as facts. The criticism that can be levelled against this book is that it does not make the reader fully aware of the controversial nature of the present data. In an earlier book (*The Unity of the Universe*, Faber, 1959), Dr Sciama advanced several attractive arguments in support of the steady state theory. Are the present observations really so unequivocal as to warrant a change of view?

Cosmology was (and even now sometimes is) regarded with suspicion by workers in other branches of science for its lack of actual data and its wealth of ingenious theories. It is hoped that by acquainting the sceptic with the very wide scope of observational cosmology today, this book will correct that impression and will thereby serve a useful purpose.

J. V. NARLIKAR

CORRESPONDENCE

Doomsday Syndrome

SIR,—In the article by John Maddox on "The Doomsday Syndrome" in *Nature* for September 3 (**233**, 15; 1971) it is said that the current alarm about the effects of exhausts from supersonic aircraft on ozone levels in the stratosphere is quite unfounded. It seems to me that this statement does much less than justice to the calculations by Harold Johnston (*Science*, **173**, 517; 1971). His very sober and detailed calculations of course involve a very complicated set of equations. He may have made errors, or may have overlooked some factors, as he himself is careful to admit. It would seem to me that Johnston's calculations are an excellent example of the proper use of basic scientific knowledge in considering the impact of a new technological development. Like any scientific contribution, this is open to criticism and revision; but surely it is far better to raise these issues, and thrash them out, before building a fleet of commercial SSTs rather than after.

As to Mr Maddox's larger thesis, I am not one of those who is crying out "Doom within the Decade", but as far as keeping the world a livable place is concerned I regard present trends as extremely ominous. As one example, I suspect a survey of the world would show a steady increase, over the last half century and more, in the amount of land that is becoming desert or semi-desert. The Israelis, of course, are reversing this trend in their own small country; but the net trend, on a world wide basis, seems certainly to be for the deserts to increase. I spent nearly three months in Australia last year, and enjoyed it immensely; but the more thoughtful and well informed Australians evidently think that this is happening to them. It has certainly happened in the Middle East, in many parts of the Mediterranean Basin, and elsewhere, throughout the course of human history; but I suspect that modern technology, and the need of feeding a rapidly rising population, are accelerating the process. I want to see mankind develop a world that will be at least as good to live in a hundred years hence, or ten thousand years hence, as it is today. I am not giving way to despair, and I believe in working to change what I see as the present trends; but I cannot be an optimist.

Yours faithfully,

JOHN T. EDSALL

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Research and Development

SIR,—Professor S. Luria's assertion (*Nature*, **233**, 171; 1971) that the only option for control is at the level of development of technology and not of basic research should be accompanied by a clarification as to who should be responsible for the control. Should general citizens participate in the decision-making (and I believe they should), then they could do a proper job only if the possibilities of innovations emerge from the basic research at such a slow rate that they can keep up with the ideas about novel developments in science. Otherwise, the development of technology cannot be properly assessed.

As regards the control of basic research, these days most of the scientists cannot conduct the work on their own private funds, and some organizations are required to allocate public money to individual scientists. Since there are always more competent scientists with curiosity and more ideas than available funds, some sort of control has been, is, and will always be exercised. The crucial point then does not lie in the unrealistic question as to whether or not to impose a control on basic research, but what type of control should be chosen for whose benefit on both research and development.

Yours faithfully,

A. SIBATANI

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Insecticides

SIR,—Of three articles on insecticides in *Nature* of October 15, 1971 (leader on "DDT may be good for people" on page 437, Norman Borlaug's support for the pro-DDT lobby on page 444, and "Pyrethrin prospects" on page 441), the last will be the most encouraging to many biologists. Your leader and Norman Borlaug appear to miss one important point—that the proposed banning of DDT in the USA will stimulate the search for better insecticides and integrated pest control which involves biological as well as chemical methods adapted to the ecosystem concerned. Efforts in these directions remain at a relatively low ebb so long as the bludgeon of DDT and other persistent synthetics is readily available. In the words of IBP's Working Group on Biological Control which includes a number of leading specialists on pests and which met in September 1971 at Canberra, there is "increasing realization that the recent era of nearly sole reliance on pesticides for insect control has been a major failure—due to the attendant problems of pesticide resistance, inducement of secondary pest species, the ever-increasing need for more pesticides (pesticide addiction) and mounting costs, yet poor insect control and severe harm to non-target species and the environment. In short, a more ecological approach has become a recognized necessity".

Few would go so far as to recommend the banning of DDT on a world basis until better methods become available and cheap. The present day leaders of developing countries are really too intelligent to follow the example of the USA blindly, as Borlaug suggests they would.

Yours faithfully,

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Should books be prohibited on the grounds that such a step would stimulate the search for better methods of communication ?—Editor, *Nature*.

Announcements

University News

The personal title of professor of parasitology in the **University of Birmingham** has been conferred on **Dr J. Llewellyn.**

Lord Todd of Trumpington and **Mr J. R. Colville** have been elected into honorary fellowships in Churchill College, **University of Cambridge.**

The title of professor emeritus has been conferred on **Professor Raymond Smart,** in recognition of his services to **Heriot-Watt University.**

Dr C. P. Whittingham, Rothamsted Experimental Station, has been appointed visiting professor in the Department of Botany and Plant Technology, Imperial College, **University of London.**

Dr G. D. B. Jones has been appointed to a chair of archaeology in the **University of Manchester.**

Dr S. W. Glover, MRC, Edinburgh, has been appointed to the chair of genetics in the **University of Newcastle upon Tyne,** and **Dr F. Goodridge** has been appointed to a personal professorship in electrochemical engineering.

Dr T. H. Hanna has been appointed professor of civil and structural engineering in the **University of Sheffield.**

Dr D. H. Wright, University of Birmingham, has been appointed to the chair of morbid anatomy and experimental pathology at the **University of Southampton.**

Appointments

Professor R. C. O. Matthews, University of Oxford, has been appointed chairman of the **Social Science Research Council** in succession to **Mr Andrew Shonfield.**

Dr Max Milner has been appointed secretary of the **Protein Advisory Group of the Food and Agriculture Organization.**

Miscellaneous

Professor Preston E. Cloud, University of California, has been awarded the **Paleontological Society medal,** in recognition of his research in the biological aspects of Earth history.

The 1971 **Van den Berghs and Jurgens nutrition awards** have been won by **Mr R. J. C. Stewart,** London School of Hygiene and Tropical Medicine, **Dr C. R. Paterson,** University of Dundee, and **Dr J. K. Howard,** Liverpool Health Department.

Entries are invited from candidates under thirty years of age for the **1972 Maccabaean prize,** which will be awarded for an essay on some aspects of the history of medicine or pharmacy. Further information can be obtained from Dr J. K. Crellin, Wellcome Institute of the History of Medicine, 183 Euston Road, London NW1.

International Meetings

November 16–17, **Government, Industry and the Environment,** London (British Institute of Management, Management House, Parker Street, London WC2B 5PT).

November 22–29, **Bulgarian Science and Technology,** London (Sam Black, London Chamber of Commerce and Industry, 69 Cannon Street, London EC4N 5AB).

November 23–25, **Hazards in Construction—an Examination of Causes, Consequences and Costs of Accidents,** London (Conference Office, Institution of Civil Engineers, Great George Street, London SW1).

November 25–26, **Primate Behaviour,** London (Dr R. P. Michael, Primate Behaviour Research Laboratories, Institute of Psychiatry, Bethlem Royal Hospital, Monks Orchard Road, Beckenham, Kent).

November 29, **Practical Data Preparation,** London (Conference Department, The British Computer Society, 29 Portland Place, London W1N 4AP).

December 1, **Non-destructive Testing,** Harwell (Dr P. Hawtin, Chemical Engineering Division, Building 351.15, AERE, Harwell, Didcot, Berkshire).

December 15–17, **Organisms and Continents through Time,** Cambridge (Dr C. P. Hughes, Department of Geology, Sedgwick Museum, Downing Street, Cambridge CB2 3EQ).

Errata

In the News and Views article "Living Longer" (*Nature*, **233**, 162; 1971), the two statements attributed in the eighth paragraph to Dr R. D. Clarke were communicated by Dr R. W. Prehoda.

In the article "Role for Ferredoxins in the Origin of Life and Biological Evolution" by D. O. Hall, R. Cammack and K. K. Rao (*Nature*, **233**, 136; 1971), Table 1 should read as follows:

Table 1 Amino-acid Composition of Type 4 (Plant) Ferredoxins

Amino-acid	1	2	3	4	5	6	7	8
Lysine	3	5	4	4	4	5	5	4
Histidine	1	1	1	1	2	1	1	1
Arginine	1	1	1	1	1	1	2	1
Tryptophan	0	0	0	0	0	1	1	1
Aspartic acid	13	14	12	9	14	10	11	13
Threonine	7	6	10	7	6	6	4	8
Serine	6	7	8	8	8	8	7	7
Glutamic acid	13	15	10	16	9	15	16	13
Proline	4	3	4	4	5	4	5	4
Glycine	12	6	7	9	9	9	6	6
Alanine	9	11	10	6	7	6	7	9
Cysteine	5	4	6	4	5	5	5	5
Valine	4	6	5	6	5	10	6	7
Methionine	1	1	1	1	2	0	0	0
Isoleucine	6	5	3	5	6	4	4	4
Leucine	9	9	7	8	7	6	10	8
Tyrosine	3	4	4	2	3	4	3	4
Phenylalanine	1	3	3	4	4	2	3	2
Total amino-acids	98	101	96	95	97	97	96	97
References	*	23	24	18	25	26	27	28

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Mrs Thatcher and the Universities

THOSE who may have hoped that the months ahead would see a better relationship, or at least a more logical relationship, between the British government and British educational institutions will have been disappointed by the exchange last week in the House of Commons between Mrs Margaret Thatcher, Secretary of State for Education and Science, and the robust company of her critics and lukewarm friends at the end of the debate on the Queen's Speech which outlined the British government's programme of legislation for the year ahead. The first thing to be said, of course, is that there is now very little chance of any but comparatively minor administrative changes in the way in which young men and women in Britain are educated. The school-leaving age will be raised to 16, but that has been on the cards for several years. The Queen's Speech (written by the Prime Minister and his colleagues) says that "provision for higher and further education will be improved and expanded", but there is very little in the record of the debate on November 5 which suggests that those words are more than platitudes. To be sure, Mrs Thatcher roused to anger some of her most fierce critics by announcing the decision that in future students' unions would have to look for support to their universities and not to the local authorities accustomed to pay fees, but that is hardly a matter on which critics have temperate things to say. And the sad truth is that Mrs Thatcher herself contributed nothing to resolving the doubt which still surrounds the future of the British university system and its relationship with the other instruments of higher education.

Why should this be? Is the British government entirely powerless in the management of its own affairs? For the past six years, the previous Labour government was occupied in making water flow uphill by advocating the binary system of higher education, a mixture of universities and polytechnics. At this stage, nobody can know whether the intention was to discover a cheaper way to higher education than that of the traditional universities, a more egalitarian formula for the admission of students or genuine diversity. The fact is that by setting out to create polytechnics, the British government appeared to wash its hands of the universities. But it is clear that the polytechnics, dependent as they are on local rates and taxes, are also outside the government's ken. Paradoxically, it was the Labour government that found what now appears to be a formula for shrugging off the obligation of central government for higher education. In spite of the painful anomalies which suffuse the relationships between polytechnics and universities, it is perhaps only natural that the present government should put up with them for the sake of a quiet life. The trouble, of course, is that both parts of the binary system at present exist in a kind of limbo, not knowing what will happen next. On last Friday's form, neither partner in the binary system would be advised to look to Mrs Thatcher for guidance. She had literally nothing to say on this important issue. Her best defence is that most of her potential critics seem to have been so bemused by issues such as the proposal to strengthen the financial position of direct grant schools and to undermine the automatic autonomy of students' unions that they had nothing to say about the central issue of how best to organize higher education.

The sad truth is that there is no reason why Mrs Thatcher should be at a loss to know what now to do. First of all, of course, there is a certain arithmetical inevitability about the pattern of higher education. Each year, more students find their way into universities and polytechnics. Although governments are inclined to take the credit for the pace of this expansion, it happens to be a kind of historical necessity that the university population should grow at such a rate as to double in just over a decade. Eventually, of course, when most of the population finds its way into higher education, the pace of growth will slacken, but for the time being any British government is bound to a kind of chariot wheel that will not stop turning until the 1980s are over. To claim credit for this is like boasting at having arranged sunrise at some previously advertised time of day.

What Mrs Thatcher really needs to tackle is the question of how to pay for higher education and, in the same spirit, how to organize it. First of all, it is anomalous and debilitating that universities and polytechnics should be organized quite differently, with central government funds for one and local authority funds for the other. Why not amalgamate the two elements in the binary system? Second, it is absurd that instruments such as the University Grants Committee should be dedicated to the rule that all institutions of the same category must be counted equal. This spurious egalitarian spirit was a serious source of discontent about the university system when there were only universities to worry about. It would have been better for the health of university education if it had been easier for universities with ambitions in, say, classics or photography to pursue their particular interests without the fear that they might fall foul of the University Grants Committee and its improving standards. To be sure, such independence from preconceived notions of what a university should be is only possible when universities themselves raise at least a part of the money they have to spend. The moral for Mrs Thatcher is that the health of higher education as well as the administrative convenience of her administration require that there should be not so much a binary system of institutions but a binary system of sources of finance. In practice, this requires higher university fees, paid for by local authorities, more independence for polytechnics, more responsibility by individual institutions for determining what constitutes a decent course in higher education and a greater sense among students that the whole thing is worth having, whoever pays the subvention for the students' union. Why is it that Mrs Thatcher seems entirely to have shrunk from that simple declarative position?

The Importance of William M. Magruder

LESS than a year ago, even Mr William M. Magruder's fondest admirers, of whom there are many, must have been downcast at the collapse of his campaign to persuade Congress to sponsor the supersonic transport aircraft project. Even at the time, it seemed as if a more subtle person might have been more successful. Mr Magruder has a reputation as a salesman of new ideas, but he is a high pressure salesman—the kind of man who tends to begin his sales pitch by jamming his foot in the door. It is no wonder that Congress's unwillingness to stomach the SST was if anything strengthened by the sense which Mr Magruder gave a great many senators that there were no options open to them. In retrospect, it is of course extremely strange that such an experienced operator as Mr Magruder should have failed to anticipate the consequences of a refusal by Congress to vote the money for which he asked. Yet, to the Administration's chagrin, there appear to have been no contingency plans. Lesser men than Mr Magruder would no doubt have quickly found themselves banished to the outermost regions of the United States. It is therefore something of a surprise that Mr Magruder has now emerged as the head of what is called the New Technological Opportunities Program, a still somewhat amorphous scheme for winning public benefits of various kinds from the opportunities which technology now provides.

Quite apart from the question whether Mr Magruder is the right man for such an intricate job, the decision to set up a White House organization for the exploitation of technology raises all kinds of difficult problems, both in the management of the United States government's interests in science and technology and in the process of forming an accurate appreciation of what science and technology may do for a society such as that of the United States. The most obvious line of speculation since Mr Magruder's new job became known is the extent to which disappointment will cut across the operations of the Office of Science and Technology, hitherto the principal channel for the coordination of the federal government's activities in the support of basic science and in some fields of technology as well. From Dr Edward David down, the air has been thick with loyal protestations that the new arrangements imply no diminution of authority for the Office of Science and Technology and some have even said that there will be benefits in having Mr Magruder at the White House to lend support to projects which seem to have a technological flavour of some kind. Unfortunately, however, the situation is a good deal more complicated than that. In the past few years, the Office of Science and Technology has done a great deal to strengthen the representation of agencies such as the National Science Foundation in the annual competition for budget appropriations.

The biggest danger now is that Mr Magruder, busy as a bee as is his habit, will muddy the waters unnecessarily. Even in the United States, there are serious limitations to the uses which can be made of technology. People say, quite rightly, that the threat of another earthquake in San Francisco is sombre, that the prospect of hurricanes each autumn is an affront against human dignity and that it should somehow be possible to get rid of the constant embarrassment about the balance of payments by wringing a little more blood out of the stone of technology. The trouble, alas, is that there is no easy way of knowing precisely when it is possible by means of a strictly technological development to make wishes into realities. The objection to much of what has in the past few years been said of the power of technology to cure social ills of various kinds is that the wish has been the father of the thought. The truth is, of course, that even when it is acknowledged that cancer, for example, would be best got rid of, or when society as a whole yearns for the removal of earthquakes, there is a limit to the amount of money which can be usefully spent in the attainment of these desirable objectives. The danger now is that Mr Magruder's brash new broom will be sweeping away energetically for a good time before this simple lesson has been re-learned. The result will be, if the worst fears are fulfilled, that the cause of rationality in the applications of technology to practical problems will have been set back by several years. Will Mr Magruder be more perceptive in his handling of this question than in his dealing with the supersonic transport?

100 Years Ago

But the most interesting, perhaps, of all the subjects with which the *Académie des Sciences* busied itself, was that of seeking an economical means of alimeniation for the inhabitants of Paris during the siege. Given certain limited sources of supply, a fixed amount of suitable organic matter, and the problem was how to use the same to the fullest and most profitable degree. Of sheep and oxen there was but an exceedingly limited provision in proportion to the very populous state of the city, and although corn and wine were said to be in abundance, there is no doubt the authorities were from the first sorely troubled by the vague estimates that were published of these comestibles.

A proposition to manufacture artificial milk, brought forward by M. Gaudin, seems worthy of some notice. That gentleman estimated that 500,000 litres per day of milk could be prepared in Paris at an exceedingly trifling cost, which should have all the nutritious qualities of good milk, and which should, besides, be neither unpleasant of taste or smell. An emulsion at a very high temperature is made of *bouillon de viande* prepared from bones, fat, and gelatine, and when cold, a product is obtained resembling in taste stale milk of a cheesy flavour; the components of ordinary milk are all present, the gelatine representing the casein; fat, the butter; and sugar, the sugar of milk. For admixture with coffee, chocolate, soup, &c., the milk is said to be by no means disagreeable.

Many propositions were brought forward to economise the blood from the abattoir, the plan suggested by M. Gaultier of mixing it with flour in the manufacture of bread being perhaps the best and simplest, as the fibrine and albumen, so rich in nitrogen—of which the alimentary properties are well known—are in this way utilised to the highest degree. Less inviting is the proposal of M. Fud to consume the carcases of animals that died of typhus, rhinderpest, and other diseases, the flesh in these instances being, so asserts M. Fud, capable of use as food, if only cooked in a suitable manner.

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OLD WORLD

TELEPHONES

Anachronism on the Way

from a Correspondent

THE British Post Office has surprised nobody and disappointed many by finally deciding on a large analogue switching system for its telephone exchanges in the late 1970s and early 1980s. The system, called the TXE-4, has been under development by Standard Telephones and Cables Ltd, one of the Post Office's traditional equipment suppliers. But as the TXE-4 handles analogue signals only, it cannot mesh with the pulse code modulation digital transmission systems which the Post Office is installing and boasting about. As there is no doubt that the telephone system will eventually be all-digital—as it must be to handle computer data, television and voice signals indiscriminately at high speeds—the TXE-4 is, before it is installed, an anachronism. To adopt it for the future is like adopting a design of traffic roundabout that cannot accept traffic from the latest motorways.

But the Post Office, like the heart, has its reasons. The chief advantage of the TXE-4 is that it will speed the replacement of the old-fashioned Strowger switching on which 95 per cent of the national telephone system still depends. The TXE-4, based on reed-relays, is a semi-electronic exchange. It can provide up to 70,000 lines—the size of a large local telephone exchange—and resembles the TXE-2, the smaller semi-electronic exchange which the Post Office is already ordering at the rate of three a week. This type of switching is the only system available that is truly compatible with the existing Strowger. Moreover, it is ready, or almost ready—STC has one developmental model working (although at costs that are nowhere near competitive with Strowger exchanges). The £15 million contract that the Post Office has given STC will allow the company to put the TXE-4 into production and to give the Post Office, under this contract, eighteen of them.

Mr Edward Fennessy, managing director of Post Office telecommunications, has conceded that in making this major and long-deliberated decision, the Post Office may be accused of over-conservatism. So it might. There had been hopes that the Post Office would decide on a computer-controlled switching system, preferably an all-digital one. But to do so would have meant a delay of several years. The enthusiasts for the TXE-4 say that it can be computer-controlled when the need arises and that it will therefore not be obsolete—merely obsolescent when the all-digital communications network arrives. The Post Office clearly has bent over backwards to avoid repeating the disastrous mistake of the 1950s—the decision to go for all-electronic switching without an intermediate stage. It is being super-cautious, and perhaps the chance for practical immediate improvements to the existing telephone network will justify it.

But exchange equipment is big business, one which gave British telecommunications manufacturers the leading position in world markets. Nobody abroad is going to buy the TXE-4, it seems safe to say. It is too eccentrically British to have much appeal abroad. (The expense of its development has been rebuked by the Committee on Public Accounts.) Neither will it achieve another objective supposedly held by the Post Office—to stimulate competition. If in December 1972 the Post Office decides to install the TXE-4 on a major scale, STC will probably teach GEC-AEI and Plessey how to make it. Thus the old circle of suppliers—the ring—will be just as closed to outsiders as it was before Parliament asked the Post Office to act as a real business in the outside world. The alternative would have been for the Post Office to buy large semi-electronic exchanges abroad and let the British industry get on with the development of the more advanced computer control exchanges which the Post Office will need very soon and which have great export potential.

RESEARCH AND DEVELOPMENT

Small Firms Seedbed

THE theme of the Bolton report published last week is that the British Government should remove the inequalities and disabilities from which small firms now suffer (*Report of the Committee of Inquiry on Small Firms, HMSO*, £2.55). "Benign neglect" is how Mr J. E. Bolton described the government's attitude to small firms so far, and the government's immediate response has been the establishment of a small firms division within the Department of Trade and Industry, as the Bolton report requested.

Deep in the 436 pages of the report are its findings on research and development in small companies (broadly speaking, companies with less than 200 employees), based on one of the eighteen research reports commissioned by the committee (see *Nature*, **233**, 226; 1971), but the committee has considered other sources and arrives at some conclusions.

The committee scorns the suggestion that new ideas are excessively costly for small companies to pursue, pointing out that small companies "continue to make major inventions . . . even in the areas of the most advanced technology". The committee goes on to say, however, that "they cannot possibly play a major innovative, as distinct from inventive, role in activities requiring very large numbers of employees and capital such as airframe manufacture". While warning that the statistics available must be interpreted with caution, the report concludes that, on the question of invention as distinct from innovation, small companies "make a disproportionately large contribution, particularly in relation to their expenditure on research and development". The increased costs of research and development are not seen to be a contributory factor to the overall decline of the small company which the committee notes, as costs are in general highest in industries which are already concentrated—for example the aerospace and chemical industries. The greater availability of research facilities from industrial research establishments, government establishments and universities is making research easier for small companies and the report says that there is ample evidence that economic growth is impaired more by a failure to apply existing knowledge than by shortcomings in new research and development.

None of the report's sixty recommendations relates specifically to research and development in small companies, but the general tenor of the report is to make life easier for them and this can only encourage their inventive work. That the Bolton committee considers this aspect of their work to be important is shown by the last three of the eight functions of small firms that the report distinguishes, namely

- that small companies, although they account for a small proportion of expenditure on research and development, are an important and low-cost source of innovation in products, techniques and services,
- that small companies are a breeding ground for new industries—that is for innovation writ large,
- that small companies are the seedbed from which new large companies will grow.

In a statement on the report, Mr Bolton, the committee's chairman, said that "this seedbed function appears irreplaceable" and that the most important question which faced the committee was whether small companies will "survive and flourish in sufficient numbers to continue to provide the seedbed of new enterprise".

NUCLEAR POWER

Which Way to Turn?

A REASONED plea is made in the latest issue of *State Service*, the journal of the Institution of Professional Civil Servants, for the British government to adopt the Steam Generating Heavy Water Reactor (SGHWR) as the next step in the British nuclear power programme. Mr John Lyons, deputy general secretary of the IPCS, says that electricity generation would be cheaper and export potential higher if the SGHWR were adopted instead of the Advanced Gas Cooled Reactor (AGR) which the British government is at present supporting.

The Department of Trade and Industry is studying the next step in an official committee. The question is whether to continue with the AGR or to adopt the SGHWR. The committee is also considering whether the High Temperature Reactor (HTR) or the American light water reactor could be used as the basis of British nuclear power generation until the fast reactor, now under development, is phased in. Mr Lyons dismisses the possibility of using the American light water reactor as, in his view, the British reactors are better than their American counterparts.

The HTR on the other hand is the reactor actively under consideration in Britain as the next step after the AGR. Its development is, however, seven or eight years behind that of the SGHWR, now ready to go into production. The decision therefore boils down to whether to continue building AGRs until the HTR becomes a practical possibility—and there is no guarantee of this—or to abandon the AGR and base the British nuclear programme on the SGHWR for the next ten years. Mr Lyons emphasizes that a decision to adopt the SGHWR would not mean relinquishing the HTR and he says that development work should continue.

The reasons for replacing the AGR by the SGHWR are, according to Mr Lyons, three-fold. First, the capital cost and cost of electricity generation by the SGHWR will be substantially less than that of the AGR. Second, the SGHWR is better able to follow the demand for electricity and simpler to construct and maintain. It also produces more plutonium—an important factor for the fast reactor programme. Third, the SGHWR has a high export potential whereas the AGR has none.

Mr Lyons points out that the decisive factor which should make the committee recommend the SGHWR is its export potential. It remains a sore point that Britain has only exported two nuclear power reactors—both of them of the Magnox type. Mr Lyons argues that once a country has invested in a water reactor, it is more likely to continue with a similar type. Thus the SGHWR is more likely to be sold abroad than the AGR which Britain has completely failed to export so far.

Mr Lyons also demonstrates his lack of faith in the British ability to maintain its two-year lead in fast reactor development by saying that when the time comes for Britain to export its fast reactors, the Americans and Europeans will have caught up, and unless Britain has a footing in the export market by then it will be severely handicapped.

The Central Electricity Generating Board has so far snubbed the SGHWR although, according to Mr Lyons, the chairman, Sir Stanley Brown, has acknowledged its suitability. The CEGB has opted for the HTR to follow the AGR because it is more likely to have an edge over the SGHWR in the larger reactors that the CEGB will need. Also part of the argument for continuing with the AGR for the next few years is that the CEGB staff are trained in gas reactors and that the introduction of a water reactor would mean acquiring a new technology.

HOVERCRAFT

Lift-off

from a Correspondent

Static tests are now under way on Britain's hovertrain after four years of development by Tracked Hovercraft Ltd. Running tests will be made on the mile long track at Earith near Cambridge in a few weeks' time.

Two British developments form the basis of the hovertrain. The jet air cushions supporting the hovercraft were pioneered by Sir Christopher Cockerell and the propulsion system is a single sited linear induction motor invented by Professor Eric Laithwaite of Imperial College, London. The combination of hoverpads and linear motor will allow operational speeds of up to 300 mph. The propulsion system itself is quiet and the noise from the air pad fans is not excessive, although at present the RTV 31 test vehicle is fitted with unsilenced fans so that noise sources can be easily located. A progressive noise reduction programme is aiming at 90 db—comparable to a heavy lorry—as an acceptable noise level. The test vehicle is remotely controlled with the equipment on board telemetered by the control centre. A second experimental craft is nearing completion and the two vehicles will be used for future development of the suspension, propulsion and guidance systems.

A further grant of £1.75 million in addition to the £3.6 million already loaned to THL was confirmed by the British Government in September and this will allow the extension of the elevated track from three to eight miles so that speeds of 250 mph should be reached by the end of 1972.

Interest in the hovertrain is rapidly increasing. Within the past month the United States Department of Transportation has officially endorsed the British system for the congested north-east corridor—the Washington–New York–Boston run. Tracked Hovercraft Ltd is convinced that the key factor in the cost of hovertrain systems, which are also being developed in France and the USA, is the cost of the track. The American system uses a U-shaped trough whereas the British system uses a simple box beam and cost analysis of the two systems showed the THL system to be cheaper by 20 per cent—a saving of $700 million over the projected route. The department's report recommended that planning of the route should begin immediately and that the decision on which system to use should be made in 1976.

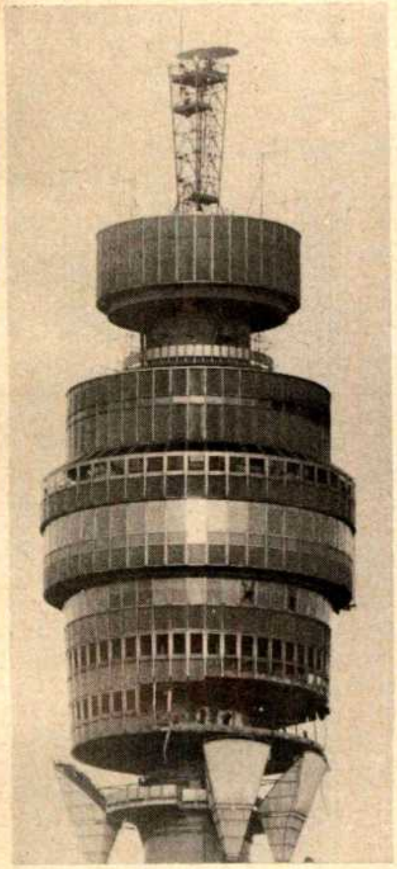
THL has also studied the possibilities of hovertrain links between London and Foulness, Gatwick and Heathrow, and between London and Liverpool. It estimates the cost over a 200 mile run, including stations, vehicles, construction and land acquisition, to be appreciably under £1 million per mile, the cost of motorways. A commercial application of the hovertrain would operate on pylons spaced up to 150 foot apart and 25 to 30 foot off the ground which eases the cost of land acquisition and causes less disruption than motorways. THL also estimates that the service could be run at a 10 per cent return on capital invested at rates between British Rail's first and second class fares.

THL claims, and the rest of the world appears to be beginning to agree, that its system is faster, quieter, cheaper and simpler than its French and American rivals and it is confident that, provided no unexpected snags appear during testing, the hovertrain is both a practicable and an economic proposition for long distance links.

Appointment

Professor S. F. Edwards, University of Manchester, has been appointed by Mrs Margaret Thatcher, Secretary of State for Education and Science, to fill one of two outstanding vacancies on the University Grants Committee. His term of office will run until 1976. The other members are Sir Kenneth Berrill, chairman, Sir Robert Aitken, Professor G. A. Barnard, Professor C. E. H. Bawn, Professor J. Black, Dr G. S. Bosworth, Miss E. J. Bradbury, Professor A. J. Brown, Dr D. Cook, Professor R. C. Cross, Professor J. Cruickshank, Professor A. Davies, Professor J. Diamond, Mrs J. Floud, H. R. Galleymore, Professor N. C. Hunt, Professor D. Lewis, Professor P. G. Stein, and Professor Sir Charles Stuart-Harris.

Experimenters Incommunicado



THE characteristics of the Post Office Tower in London under stress have, as is well known, been tested in a recent experiment, the authorship of which is at present unknown even to the London police (see picture). It is less well known that a more carefully controlled study of the building has been carried out by the staff of the Building Research Station and recently published (*Strain Measurements at the GPO Tower, London,* K. J. Eaton and J. R. Mayne, CP29/71). The lack of communication between the two groups of experimenters will no doubt be regarded as a further sign of interdisciplinary isolation.

STANDARDS

All Things being Equal

THE International System of units (SI) was rounded off for the time being by the decisions of the 14th General Conference of Weights and Measures (CGPM) in Paris last month. The conference agreed that the mole should become a base unit of substance within the SI with the pascal and siemens being approved as SI units of pressure and conductance, a pascal being equal to a newton per square metre and a siemens equal to a reciprocal one ohm. The CGPM's forty member states meet at least once every six years to make decisions about units, but its function is really to approve the work of the International Committee on Weights and Measures which meets at least once every two years. Once approved, SI units are published by various bodies throughout the world and by the British Standards Institute (BSI) and HMSO in Britain.

They are also published by the International Organization for Standardization, the international authority on names and symbols for physical quantities and the relation between quantities and units. Seven parts of ISO recommendation R 31 have so far been published on quantities and units, with three parts passed for publication and four more in draft.

Before publishing a recommendation, ISO consults national standards organizations and other interested bodies such as the International Union of Pure and Applied Physics, the International Union of Pure and Applied Chemistry and the International Electrotechnology Commission, all of which have their own committees working on standardization of language, symbols and units, and ISO often takes over their agreements. By the time a standard is published it will have been commented on at least two or three times by the interested bodies of the forty or so countries that participate in ISO. As a result, about ten years elapse from the beginnings of agreement on a standard to publication. But the proposed new standards are published and tend to be used before they are officially approved—as has been the case with the SI pascal and siemens.

The future of standards lies simply in efforts to reach greater agreement and in deciding on units and symbols for new fields of science, although, according to Professor McGlashan of the University of Exeter and IUPAC, "more progress has been made in the past twenty years than in the previous ten thousand".

The next meeting of the CGPM in 1975 will celebrate the centenary of the signing of the Metre Convention and it is unlikely that there will be any change made in the base units of SI. The basic work seems over for the moment, but work will no doubt continue in the redefinition of standards—for example the 10th conference in 1960 redefined the metre as "the length equal to 1,650,763.73 wavelengths in vacuum of the radiation corresponding to the transition between the levels $2p_{10}$ and $5d_5$ of the krypton-86 atom," replacing the definition of 1889 based on the platinum-iridium bar.

WORLD WILDLIFE

Only Skin-deep

IN the presence of such personalities as Sir Charles Clore, Lady Gage, Miss Iris Murdoch, the editors of *Vogue* (both British and American versions), Mrs Rolf Harris and two buyers from Harrods Ltd, Aquascutum, in collaboration with the World Wildlife Fund, revealed its collection of simulated fur fashions earlier this week.

On display, suitably draped around six of the potential Miss Worlds, to the accompaniment of recorded jungle drums and lashings of champagne, were coats made from simulated cheetah, leopard, ocelot and tiger in "styles created especially to celebrate the 10th Anniversary of the World Wildlife Fund". A number of puma and tiger cubs imported for the occasion—presumably to show what the real thing looks like—started off by gambolling around and ended rather frightened at the pressing enthusiasm of their well-wishers.

Mr Peter Scott, chairman of the British National Appeal, opened the proceedings by saying that he hoped the wearing of real fur will die out as a fashion (cheers), that the Ministry of Defence has agreed not to buy real fur for military drummers to wear (patriotic cheers) and that the sale of the synthetic furs would help conserve those predatory species in danger from man (yet more cheers).

The coats, from man-made fibres cost less than £40 compared with £1,200 to £2,000 for a real ocelot coat. How much do the simulated coats cost to make? Well, Aquascutum for one isn't saying, but judging by the number of women surreptitiously trying them on at the end, they are going to be quite the thing to be seen in. Were they as good as the real thing? Well, no, of course not," said one eager purchaser, slipping out of a (simulated) leopard into a (simulated) cheetah, "but one's friends won't talk to one if you wear real fur; I mean when there are only 200 left in the world you're not going to be very popular if you appear wearing five of them, are you? "

Meanwhile, back on the dais, Miss World 1969—Miss Eva Reuber-Staier—wearing a (simulated) jaguar coat was playing with the young cats to the delight of the adoring multitudes and the frantic photographers—"a little more leg, Miss Ruber-Staier? ". Cameras flashed, people cooed, and Peter Scott signed autographs in a corner—simulated fashion furs had definitely arrived.

And if the cats seemed less delighted than the models at the bright lights and brighter people, can you really blame them?

EUROPEAN SPACE

Success and Failure

THE past few weeks have seen some ironical developments for European and British space research. Britain, which no longer wants a national launch vehicle, now has one, and ELDO is still without the launcher which is the chief purpose for its existence. The avowed British policy of depending on the United States for future launch facilities, both for scientific and technological satellites, has, however, now been vindicated (at least partially). At last, the anomaly of continuing with this inadequate British launcher, contributing to ELDO and planning to make increasing use of American facilities has been resolved, and the situation is now less confused than at any time since Britain joined ELDO while at the same time developing Black Arrow.

Black Arrow's successful launch, on October 28, and the failure of Europa II on November 5 lend weight to the British decision to stop financial support for ELDO. Coming only a few days after the announcement that the US State Department has now agreed in principle to provide launch facilities for research, meteorology, navigation, telecommunication and Earth resources satellites, the most recent failure may well sound the death knell for ELDO. The only members of the organization still enthusiastic about an independent European launcher are France and Germany, who may proceed with a binational programme aimed at providing a launcher for Symphonie.

Just what did go wrong with Europa II? It is too soon to be sure, but indications are that the failure—possibly an explosion—occurred 150 s after take-off in the first stage, Britain's Blue Streak. This is the only stage which has never failed on previous ELDO launches. But the rocket's navigation system also failed, before the explosion and, apparently, independently of it. A second explosion, in the French Coralie second stage, may have been triggered by the Blue Streak failure. It is a sobering thought that roughly 100 proved American launchers could have been bought for the £250 million spent by ELDO so far.

The future for European satellites, however, looks brighter than the gloomy launcher position might indicate. For although it has been clear for years that because the cost per launch decreases as a vehicle is used more, American launchers are and will remain cheaper than European launchers can hope to be. Until last week there was no firm promise that such launchers would be available except for scientific satellites or for projects with a large American interest, such as Intelsat. There are, however, no apparent strings attached to the new promise, although it may well be intended to create an atmosphere of cooperative goodwill towards the shuttle project.

BRUCELLOSIS

Towards Clean Cows

IN its campaign to wipe out brucellosis, an infectious disease that causes spontaneous abortion in cows and undulant fever in people, the Ministry of Agriculture last week restricted cattle movements in certain areas of Great Britain.

Although vaccination for calves has been available since the 1940s, the first real steps were taken in April 1967 with the introduction of the Brucellosis (Accredited Herds) Scheme which built up a register of herds free from brucellosis, chiefly to be used as replacement cattle for later stages of eradication. In July 1970, the Brucellosis Incentives Scheme was introduced, which provides financial inducements of £0.008 per gallon of milk for brucellosis-free dairy cattle and £5 a head in addition to the hill cow and beef cow subsidy. Both these schemes are voluntary and aimed at attracting owners of herds with light to moderate infection to build up the numbers of brucellosis-free cattle. The subsidies are paid for a five year period and one of the conditions of the scheme is that animals found to be infected are slaughtered. In November 1972, compulsory slaughter will be introduced for infected animals in those areas now subject to movement restrictions—parts of north-west England, west Scotland, south-west Wales and the Isle of Wight. Farmers in compulsory eradication areas receive £30 in compensation for a slaughtered animal, provided that the free calf vaccination service has been used since July of this year. If the service has not been used, £15 will be paid, with market value being paid for any slaughtered "contacts" (the market value of a dairy shorthorn at the end of October was £111.50). Gradually the eradication areas will be extended until the disease can, it is hoped, be effectively wiped out.

Brucellosis is not a notifiable disease and it is therefore difficult to discover how many cases there are in Britain and how much it costs the country each year. A ministry survey of 3,000 herds in 1961 suggested that between 25 and 30 per cent of herds were infected but the survey only covered dairy herds and no figures for beef herds seem to be available. In 1967 it was estimated that 14 per cent of cattle would react to brucellosis tests and in August this year a Milk Marketing Board survey over six months, using milking tests and covering every herd with which the board deals, showed that 28.5 per cent of herds contained reactors. A limited survey in Lancashire in 1970, also by the board, showed that 18 per cent of cattle reacted. There were 717 reported cases in humans in the United Kingdom and Eire last year, but it is thought that there were hundreds more either not reported or not diagnosed.

Estimates of the cost are equally vague, but a figure of £2 million to £3 million for the cost to the industry and of about £16 million to the country would seem reasonable, although the latter figure particularly is disputed.

The Ministry of Agriculture puts no official figure on the cost of eradicating the disease but something in the order of £100 million is a fair estimate. The size of this figure may account for the length of time it has taken Britain to begin eradication — some continental countries have virtually beaten the disease already, and a draft EEC regulation rules that after December 1975 no milk will be accepted from brucellosis-infected herds. The lion's share of the cost will be in compensation and incentives to farmers over the next few years. How long eradication will take depends upon a number of factors, not least the willingness of farmers to cooperate, but it is hoped to beat brucellosis in ten to fifteen years. This compares with the twenty-five years it took to remove bovine tuberculosis from 1935–60 at a cost of £130 million.

The eradication of the disease is necessarily a lengthy process as any attempt at rapid eradication would fail through a shortage of vets to carry out the work and would cause serious depletion of stocks. With a reserve of brucellosis-free animals, eradication can be managed without producing sudden shortages. The National Union of Farmers accepts that the ministry's scheme is the best approach although it is anxious that the compensation figures should be high enough—at the moment it feels that the £30 a head compensation for slaughter is not adequate because the cost of brucella-free stock to replace the slaughtered cattle is some 15 per cent higher than that for unproven stock.

Progress so far seems encouraging. The introduction of the incentives scheme has already involved 45,000 of the country's 200,000 herds and applications to join the scheme are running at about 1,500 a week. It is thought that these herds are those only lightly or moderately infected and of the 2 million or so animals tested from herds in the scheme there is a failure rate of just over 2 per cent. Due to the compensation to be paid for slaughtered animals it may be in the interests of those farmers with heavily infected herds outside the eradication areas to wait for compulsory eradication.

NEW WORLD

Conflicting Philosophies on Higher Education

by our Washington Correspondent

THE House of Representatives has done almost as much as the Senate to win friends in the colleges and universities. Like the Senate, it has departed from established traditions in voting for a huge infusion of federal money into higher education, although the proposals which have so far been agreed by each legislative body differ substantially about the method by which the largesse should be distributed. One common feature shared by the House and the Senate bills, however, is that both versions are likely to be opposed at least in part by the Administration.

The chief new provision contained in the bill which was passed last week by the House of Representatives is that federal grants would be distributed to every college and university in the United States. The bill, which was passed after four days and one night of debate, authorizes expenditure amounting to $20,000 million over five years, including $1,000 million a year on grants to institutions. Two-thirds of the institutional grants will be distributed on the basis of the number of students at each university and the remainder will be distributed according to the number of students at each institution receiving federal assistance grants.

In several respects, the bills passed by the House last week and by the Senate in August (see *Nature*, **232**, 518; 1971) represent differing philosophies on how to rescue colleges and universities from their present financial troubles. The Senate bill would set up a system of educational opportunity grants to each student, the amount of each grant depending on parental income, and it also provides for grants to institutions allotted on the basis of the numbers of students receiving these educational opportunity grants. The House bill carries these institutional support grants one stage further by also providing assistance to all colleges on the basis of their total student intake. It is that part of the institutional support provision that is likely to provide the chief stumbling block in the conference committee that must now sort out the differences between the two bills.

General institutional support is also likely to be opposed by the Administration, which favours institutional grants on the lines proposed by the Senate. The House rejected a move to knock general institutional support out of the bill, however, by a vote of 310 to 84, and the representatives of the House in the conference committee now have a clear mandate to keep the provision in the bill. The amendment to delete general institutional support from the bill was proposed by John N. Erlenborn, who argued that there is not enough evidence of financial hardship in every college and university to warrant grants to every institution, while Edith Green, chief proponent of the bill, argued that colleges and universities in the United States are "facing the greatest financial crisis they have ever seen".

In spite of their concern over the financial state of American universities and colleges, however, members of the House of Representatives removed from the higher education bill a provision for bailing out the most severely affected institutions with emergency aid. The bill originally proposed an authorization of $150 million this year and the same amount next year for such institutional support, but this was struck out on the grounds that the Commissioner of Education could not determine fairly which institutions should receive the support.

The House bill also extends the education opportunity grant system, raising the grant level from $1,000 a year to $1,500 for needy students, and extends the guaranteed student loan programme. The bill also bans discrimination on the grounds of sex for any institution receiving federal grants, but an amendment making the ban inapplicable to student admissions was carried by a small margin on the grounds that it would effectively impose federal admissions policies on the universities.

Other measures included in the bill are:

- An authorization of $5 million in 1972 for federal aid to college and university libraries, increasing to $40 million in 1976.
- Authorization for student loans at the rate of $425 million in 1972 rising to $675 million in 1975 and 1976.
- The setting up of a new National Institute of Education in the Department of Health, Education and Welfare, on the lines of the Senate-passed measure. This proposal, supported by the Administration, would have the primary function of conducting educational research.
- The bill also calls for the setting up of a special commission on the financing of postsecondary education, to report by June 30, 1973.

Although both the Senate and House-passed bills contain much that is acceptable to the Administration, they will both stick in the throat of the Office of Management and Budget because each raises the federal higher education bill much above its present level. The Senate version, for example, asks for $18,000 million over the next three years, while the House version asks for some $20,000 million over the next five years. Present funding runs at about $1,300 million a year.

Whatever the outcome of the conference, which will not take place for some time because of the difficulty in sorting out the areas in which the two massive bills do in fact differ, it is clear that the final measure will contain some provision for direct institutional support. The Senate wants such support distributed to colleges and universities whose students receive federal aid, while the House favours the major part of the federal grant money going to all universities on the basis of their total intake. Either provision would, however, be a landmark in higher education in the United States.

CANCER RESEARCH

NIH wins Round Two

by our Washington Correspondent

IT now seems almost certain that the House of Representatives will vote to give the National Cancer Institute a budget of $1,600 million during the next three years, but to keep it firmly a part of the National Institutes of Health. This is in sharp contrast to the Senate which agreed last July, by a vote of 79 to 1, to set up an independent agency devoted to finding a cure for cancer, and it means that the crucial decisions on the future organization of cancer research in the United States are likely to be taken behind the closed doors of a conference committee.

The mood of the House of Representatives can be judged by the fact that the House Interstate and Foreign Commerce committee last week agreed by a vote of 26 to 2 to send to the floor of the House the bill introduced recently by Paul G. Rogers with the relatively minor amendments tacked on by the subcommittee on Public Health and Environment (see *Nature*, **233**, 228; 1971). The support for Rogers's bill in the Commerce committee was in fact so strong that a move to amend it by striking out the word-ing and inserting the Senate-passed version attracted only four votes. But perhaps the strongest demonstration of support lies in the fact that no Republican member of the Commerce committee voted to substitute the version passed by the Senate, in spite of strong pressure from the White House. In fact, Elliot L. Richardson, Secretary of Health, Education and Welfare, took the trouble to write to every member of the committee urging them to support the Senate version.

Members of the House of Representatives will therefore be faced with a bill designed to give cancer research a greatly increased budget, and, like members of the Senate, they will not run the risk of seeming to vote against cancer research by opposing the bill. The chief challenge to the Rogers bill will therefore come from amendments designed to replace the bill with the Senate version. Mr Brock Adams, who voted against the Rogers bill in the Interstate and Foreign Commerce committee last week, is intending to introduce such an amendment from the floor of the House, and he will have the support of the White House lobbyists.

Even those who support Mr Adams's amendment, however, admit that it stands little chance of succeeding since the tide is now running so strongly in favour of keeping cancer research within the National Institutes of Health. Another reason why the amendment will not pack a very heavy punch is that the White House is in an embarrassing position over the two bills, and will find it difficult to lobby for the Senate version with any conviction. The problem is that the bill passed by the Senate is very similar to a bill introduced by Senator Edward M. Kennedy. The Administration opposed Kennedy's bill on the grounds that it might lead to the break up of the National Institutes of Health, but later came to a compromise which effectively put the Administration's name on Kennedy's proposals. The White House is therefore now urging Congress to turn down a bill whose objectives it once supported. The Administration has, however, been consistent in its wish to give public voice to its desire to aid cancer research—a great asset in election year.

SPACE

No Strings Attached

by our Washington Correspondent

One of the chief rocks on which European cooperation in space research has foundered in the past year or so has been removed by the US State Department. It was announced last week that NASA will launch European scientific and technological satellites without assurance of European collaboration in the space shuttle programme, and the US government is also prepared in principle to launch telecommunications satellites for European countries.

The State Department's offer, which was outlined in a letter from Under-Secretary of State U. Alexis Johnson to M. Theo Lefevre, chairman of the European Space Conference, may be sufficient to tempt European governments to abandon the Europa III launcher (which is designed to launch the type of satellites on which the US government has now given an assurance), thus freeing European finances for participation in the shuttle programme. The letter was sent in September, but was not made public until last week.

The new attitude of the US government marks a considerable shift in policy. For one thing, discussions of US launch policy have for the past year been underpinned—tacitly if not explicitly—by the assumption that provision of US launchers would be contingent on European cooperation in the space shuttle programme. The US government has also been chary in the past of giving assurances on the launching of telecommunications satellites that may in any way compete with Intelsat. That, at least, was one of the chief reasons advanced in Europe for pressing ahead with Europa III.

The US government is not, however, prepared to ignore Intelsat in the hope of promoting closer accord with Europe on space research, for the assurance on launcher provision is conditioned by several clauses designed on the face of things to protect Intelsat interests. Briefly, the United States will provide launch facilities for communications satellites approved by Intelsat, but blanket launch assurance cannot be given for satellites that are not supported by Intelsat.

According to the Intelsat agreement signed earlier this year, the consortium must give its advice on telecommunications satellites flown independently by member countries, the chief consideration being the extent to which the proposed satellite will compete commercially with those sponsored by Intelsat. The US government is now saying that it will launch European satellites that gain Intelsat approval, or which have been supported by the US within Intelsat. Since it is highly unlikely that satellites backed by European and United States interests would fail to gain Intelsat approval, the agreement boils down essentially to the question of US support. The agreement comes very close in practice, however, to being a complete assurance of the availability of US launchers for all types of satellites.

Whether or not such an assurance will help to sew together the tattered fragments of space collaboration in Europe is open to question, but the announcement has at least laid the basis for future negotiations between the governments of Europe and the United States. Already, the State Department has suggested that discussions should not be confined to collaboration on the shuttle, but that they should be broadened to include all kinds of space research, and two weeks ago a NASA official was dispatched to Paris to tell the European Space Conference of NASA's plans for the next ten to fifteen years. If the launch assurance is sufficient to persuade European governments that Europa III is no longer needed, such discussions would have a much greater chance of success.

NUCLEAR WEAPONS

Lessons from Cannikin

from a Correspondent

What the US Atomic Energy Commission scientists learnt from the Cannikin test on the Island of Amchitka will probably never be known, being apparently vital to national security. The lessons for all other participants in the affair are more obvious.

The drama associated with Cannikin was appropriate to a Moon shot. Environmentalists have fought during the past week a desperate court action to have papers on the environmental impact of the test released and then to use them in demonstrating that there were significant risks of earthquakes, tidal waves and radioactive leakage. On the very morning of the test, the Supreme Court sat to hear arguments on the environmental impact, and voted 4 to 3 that the test could proceed. Thereafter the AEC, clear of its last hurdle, went ahead and fired the shot which predictably triggered no earthquakes or tidal waves. It is too early to tell whether there will be any radioactive leakage, but there appears to be no concern about it.

One of the most remarkable and least noted features of this test is that in the fifties and early sixties the United States fired such shots in the atmosphere with impunity. The American public has come a long way in its attitudes since then. Unfortunately, the issues on which the AEC were challenged were in the opinion of many flimsy. It is of course an old political trick to steer clear of the central arguments and try to make the peripheral questions seem more important. The AEC did not even have consciously to pursue this policy ; the environmental question was the only one which generated a significant amount of heat. To be sure, there is never a zero risk of environmental damage and no scientist has come out with a statement that environmental arguments are nonsense, but it appears to have been the considered opinion of practically all those who studied the problem in a detached manner that the risks were very slight.

What environmentalists would desperately have liked would have been a concerted declaration from scientists warning of dangers. No such statement was forthcoming. It is indeed conceivable that the environmental movement has been harmed by the Cannikin affair. Its members may have learned the hard way that scientists with some sympathy for the movement can be alienated by a stance that scientists could not maintain. They may have lost some credibility with those middle Americans who are unimpressed when the Doomsday does not show up to order. The first callers to radio talk shows immediately after the blast were saying, "Well, what was all the fuss about then?" They may also have learnt that when dealing with politicians they are talking to pragmatic people for whom a 10 per cent, let alone 1 per cent, chance of catastrophe is acceptable. The environmentalists have to walk on a tightrope above scientists, lawyers, politicians and the general public. The Cannikin affair may have helped them to learn new tactics.

Of course, what Cannikin was really about was national security. If a good number of Senators had banded together early enough to express disbelief that this one explosion was more vital to national security than good relations with Canada and Japan, the soft centre of the Administration's argument would have been revealed. Fresh from previous insults from the new Nixon, these two countries in particular were bitter about the test and are going to be more difficult to deal with in the future as a result of it, earthquake or no. Whether the milliseconds worth of X-rays is more valuable than good relations with two allies is much the most debatable issue in the whole affair.

MARINER 9

Into Orbit around Mars

THE arrival of Mariner 9 in the vicinity of Mars today will open up a new chapter in the exploration of the solar system. If the craft successfully enters orbit around the planet, its sensors should be able to resolve some of the questions concerning the environment of Mars which have been puzzling astronomers for centuries. A spokesman for NASA predicts that there will be "a veritable information explosion about the Mars terrain, climate and atmosphere", and about its two moons Phobos and Deimos. The exchange of information obtained by Mariner 9 and by the two Russian probes also now in the vicinity of Mars will undoubtedly add to this explosion—it may be that one or both of the Russian probes is planned to attempt a landing on the surface of the planet.

Some indication of the importance of these missions is provided by the way in which the earlier Mars flyby missions changed man's ideas about the planet. It is now clear that the planet is cratered in a way similar to the Moon but that the craters are weathered and that there are also regions of apparently recent activity. Apart from straightforward photography which should produce 5,000 pictures—the 1969 mission produced 205 pictures and the 1965 mission only 22—the spacecraft carries an infrared radiometer, an infrared spectrometer and an ultraviolet spectrometer, each mounted to point at the object being photographed. In this way, the temperature, terrain and atmospheric conditions in each area pictured will be recorded.

The most interesting phenomena yet discovered on Mars are the clouds, hazes, bright spots and dust storms. A specific objective is the study of the wave of darkening observed seasonally. The spacecraft is arriving when this darkening is at its seasonal peak in the southern hemisphere. In some quarters this has been attributed to a spread of moisture from the poles with the onset of spring. A more widely held belief is that the wave corresponds to the removal of light coloured dust. Hopefully this conflict together with many others will be resolved in the near future.

One question that is not expected to be answered yet concerns the possibility of life on Mars. At present there seems little chance that any complex life forms can exist on the planet, and Mariner 9 would be unable to detect primitive life forms even at closest approach (800 miles). Recently, however, prebiotic molecules have been synthesized in the laboratory under conditions like those on Mars and it is possible that Mariner 9 could provide evidence that biological molecules are present in the Martian atmosphere.

Short Notes

Uranium Enrichment

REPRESENTATIVES of the Australian, Japanese and Canadian nuclear industries met in Washington last week with officials of the AEC and the Department of State to discuss the possibility of using US gaseous diffusion technology in multinational uranium enrichment plants. This was the first tangible sign of cooperation since the AEC announced in July that it was prepared to discuss the possibility (see *Nature*, **232**, 366; 1971). Representatives of several European countries will go to Washington for similar meetings on November 16.

It is believed that the talks centre on the possibility that two enrichment plants will be built and operated on a multinational basis—one by Japan, Canada and Australia, and the other by European interests. The chief points under discussion are safeguards to prevent nuclear material being diverted to weapons production, and the US government also wants an assurance that its enrichment technology secrets will not be able to leak out to other countries.

DDT

THE Environmental Protection Agency has decided not to suspend all uses of DDT while cancellation proceedings are going on. This allows the pesticide to be manufactured and sold throughout the United States while the EPA decides whether or not to prohibit its sale across state lines. Announcing this decision last week, Mr William D. Ruckelshaus, Administrator of the EPA, pointed out that the cancellation proceedings must be completed by March 1972, but will probably be concluded long before then. He suggested that no appreciable difference would result from any ban that could be imposed before that date.

Unemployed Chemists

EVEN those chemists who were lucky enough to find jobs waiting for them when they left the universities this summer have good reason to wish that they had graduated in a sunnier economic climate. According to a survey carried out by the American Chemical Society, their average starting salary was some 7 per cent lower than starting salaries a year ago—and, taking into account the fact that the cost of living increased by more than 4 per cent during the year, this means that starting salaries dropped by about 11 per cent compared with 1970.

But, while new graduates in employment may have to take in their belts by half a notch, many of their colleagues are much less fortunate. The ACS survey found that unemployment among newly-qualified chemists doubled from 5.1 per cent in 1970 to 10.3 per cent in 1971. First degree graduates suffered an unemployment rate of 11.6 per cent, while those with master's degrees reported a rate of 8.8 per cent and PhDs 6.1 per cent. Moreover, those who left the universities with a degree in chemical engineering found the job market even less hospitable—an alarming 12.8 per cent reported that they had not found a job by the end of the summer.

NEWS AND VIEWS

Links Between Chains

IT took probably a century of man years to decide whether myosin was two or three stranded. No sooner had the dust of that wrangle settled than another argument was on: low-molecular weight proteins were apparently shed by the myosin molecule, under conditions that led always to denaturation, or at least to loss of ATPase activity. Were these "light chains" real components of the functional molecule, or merely bound impurities? How many species are there, and in what proportion are they present on the myosin? Are they involved in the ATPase function? Does their heterogeneity perhaps arise from different populations of fibres? It may be hoped that two meticulous studies in this edition of *Nature* will help shake off the incubus of numerological uncertainty that has so long dogged the field.

Lowey and Risby (page 81) have addressed themselves to the general problem of the estimation of protein components in mixtures by gel electrophoresis. The light and heavy chains cannot be compared on a single polyacrylamide gel, because the light chains diffuse too rapidly in a gel of low concentration, whereas the heavy chains will not penetrate a gel of high concentration. Comparisons have therefore to be made between the components in separate gels, and a protein of intermediate molecular weight, tropomyosin, is added to the mixture to provide a common concentration standard for both gels. The linearity of integrated staining intensity with the quantity of protein applied to the gels was demonstrated, and the same relative concentrations of components were obtained with the use of two different protein stains. Moreover, when separated light and heavy chains at defined concentrations, based on nitrogen determination, were run on gels, the staining intensities were found to reflect faithfully the relative concentrations of the different components—a result which, not necessarily general, should give comfort to workers in other branches of protein chemistry. Using molecular weights based on mobility in gels containing the detergent SDS, the stoichiometry of all the components could then be evaluated.

The upshot is that in three fast-muscle preparations, from rabbit and chicken, each molecule of myosin gives rise to four light chains, two of a species of 18,000 molecular weight and two others of 16,000 and 20,000 respectively. It is the first kind that are liberated by treatment with a thiol-specific reagent (Ellman reagent), and their loss is not accompanied by any major change in any measured properties of the myosin, ATPase included. Slow muscles give a quite different pattern: two species of light chain are resolved, which do not correspond to any of the above components, have molecular weights estimated at 20,000 and 27,000, and are present in a ratio of two moles of each per mole of myosin. The results in terms of the number of components, and their differences, as between skeletal and cardiac myosins, are, it is agreeable to report, in substantial agreement with a recent parallel study by Sarkar, Sreter and Gergely (*Proc. US Nat. Acad. Sci.*, **68**, 946; 1971).

In red muscle it looks as though both types of myosin may be present, with five light chain components clearly discernible. The identical patterns from the muscles of two animals are particularly satisfactory features of these results, encouraging, as they do, the confidence that the stoichiometry is correct, and the heterogeneity not adventitious. Moreover, the difference between the light chains from fast and slow muscles, allied to their apparent inseparability from the myosin ATPase activity, raises the alluring possibility that they in fact regulate this function.

In the companion article, Weeds and Pope (page 85) examine the chemical relation between the various light chains. The identifying feature which they have selected is the sequence of the proteolytic fragments containing thiol groups, because these can be labelled with an isotopic alkylating agent and can thus readily be identified after electrophoretic separation of a chymotryptic digest. By this technique Weeds previously demonstrated that the inessential light chain component released by Ellman reagent contains two unique thiol peptide sequences, whereas the remaining light chains possess only one between them. Working this time with prime beef, Weeds and Pope find that cardiac (slow muscle) myosin light chains give rise in all to three different thiol peptides, one of which, a fragment of thirteen residues, is identical to the single thiol sequence present in the ATPase-associated light chains of skeletal muscle myosin.

Now the cardiac myosin light chain preparation contains two different components. Complete separation of these has not been achieved, but it seems certain that one (the larger, with molecular weight 27,000) is responsible for all three thiol peptides, whereas the smaller, of 20,000 molecular weight, most probably possesses no thiols. Sheep heart muscle myosin contains similar light chains, which give rise to the selfsame thiol sequences as those of beef heart myosin. Rabbit cardiac myosin is evidently again similar. The significance of the long common thiol peptide segment between light chains from cardiac and skeletal muscle is not obvious, for in other respects, including the molecular weight, the chains are distinctly different.

Weeds and Pope add that their unpublished results on fast-twitch and slow-twitch muscles of the cat show light chain patterns which are respectively similar to skeletal and cardiac muscle myosin. These results point once more to an enzymatic regulatory function for at least some of the light chains. The heterogeneity remains a curious feature; it may be noted that a current report (Hale and Beecher, *FEBS Lett.*, **18**, 245; 1971) has started once more the hare of heterogeneity of the heavy chains. Gel electrophoresis of the denatured chains in concentrated urea solution in the hands of these workers produces two components in equal concentration. They have done their best to control the rather extensive possibilities of chemical or physical artefacts, but workers in the field may wish to reserve judgment.

If these results are taken at face value, however, they raise now the question of whether the two components represent different halves of all myosin molecules, or different myosin populations. Much work remains to be done on myosin, but there should be no mistake about the importance of establishing the composition of the molecule in definitive terms.

SEXUAL SELECTION

Mating Preferences

from our Population Genetics Correspondent

Darwin's notebooks show that he deduced his theories of sexual and natural selection at about the same time. Sexual selection was briefly mentioned in *The Origin of Species* and discussed in detail in *The Descent of Man* published in 1871. Although direct observations of natural selection were first made around 1900, it is only in the past two decades that sexual selection has been observed experimentally. Sexual selection occurs if there are variations in the chances of mating. It usually affects the males and has always been accepted as the cause of the evolution of the special weapons such as horns and spurs used in the fighting between the males of certain species when they collect their mates.

Darwin thought that the females would also have mating preferences for particular male characteristics, especially those involved in mating displays. For a long time many naturalists refused to accept this possibility of female choice in the selection of mates, and it was left to the population geneticists to demonstrate by experiment that there were female mating preferences for males with particular genotypes. If a female *Drosophila* is placed in a mating chamber with one wild type and one white eyed male, observations show that the female will usually mate with the wild type male. But a male given a choice of wild type and mutant females usually shows no preference and matings take place with both females with equal frequency.

In experiments with *Drosophila* Ehrman showed (*Amer. Nat.*, **101**, 415; 1967; *Genet. Res.*, **11**, 135; 1968) that the mating success of the males could be frequency dependent: the females had a tendency to mate with those males who possessed the rarer genotypes for particular chromosomal inversions. In the latest issue of *Evolution* (**25**, 265; 1971), Faugères, Petit and Thibout describe experiments to analyse different components of sexual advantage. They studied the sexual vigour of the males (their ability to inseminate several females) and their success in sexual competition (the female preference for particular genotypes). They used mutant white *Drosophila melanogaster* and various wild type strains and their hybrids. Sexual competition was studied by giving the males or females either a limited choice of two individuals of the opposite sex, white and wild type, to mate with, or a multiple choice with ten flies of one sex and five of the other in the mating chamber. They then observed the copulations that took place. Sexual vigour was measured by the number of females which a male could inseminate in 24 hours.

As in previous experiments, the sexual competition affected only the males. The white males were always at a disadvantage. On the other hand, in sexual vigour, the hybrids, white and wild type, were superior to the pure strains, white and wild type. This shows that different factors are responsible for sexual selection and sexual vigour. Genotypes advantageous in sexual selection may not be advantageous in sexual vigour. Faugères, Petit and Thibout point out that the ethological factors that determine the advantage in sexual selection could be masked by other factors causing superior sexual vigour. This may affect not only sexual selection but also sexual isolation. When strains evolve sexual isolation (as in the experiments recently reported by Dobzhansky and Pavlovsky in *Nature* (**230**, 289; 1971), a particular strain evolves a mating preference within itself so that eventually matings take place only between members of a particular strain. This could be prevented if the male hybrids had a superior sexual vigour and could inseminate more females although they were less likely to be chosen as mates. If the hybrids are inferior in sexual vigour, however, the mating preferences will continue to evolve and will eventually produce sexual isolation between

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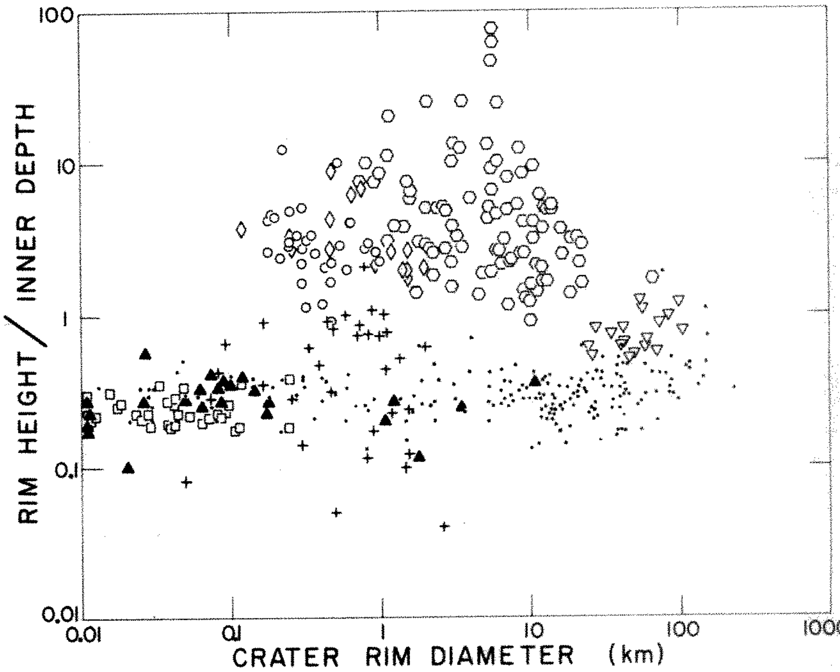
Craters on the Earth and Moon



In next Monday's *Nature Physical Science* R. J. Pike of the US Geological Survey, Menlo Park, California, classifies lunar craters according to the ratio of the external height of their rims to the interior depth of the crater floor. For normal lunar craters the ratio is usually well below unity. In other words, the floors of lunar craters tend to be below the general level of the area in which they are situated.

There are exceptions of course. Lunar craters that have been flooded with mare material have ratios of external height to interior depth of about unity, and lunar craters on cones have ratios in excess of unity.

In the figure Pike has plotted the ratio of external height to interior depth against the diameter of the crater (from rim crest to rim crest) for various kinds of lunar and terrestrial craters. The dots are what he calls "normal" rimmed lunar craters, the open triangles are lunar craters filled with dark mare material, the lozenges are summit craters on lunar domes, the hexagons are terrestrial calderas, the circles are terrestrial cinder cones, the crosses are terrestrial maars (volcanic explosion craters), the squares are experimental explosion craters and the solid triangles are meteorite impact craters on the Earth.

Pike points out that the ratio of external height to interior depth, as plotted on the figure, tends to distinguish calderas, cinder cones and lunar dome craters from normal lunar craters, maar craters, meteorite craters and experimental explosion craters, and he interprets this distinction as indicating two contrasting modes of origin. Calderas, cinder cones and, presumably, lunar dome craters are essentially constructional features formed during a series of volcanic eruptions, whereas the second group of craters seem to be characterized by formation during single catastrophic explosive events.

the strains. These would therefore have become separate species as in Dobzhansky and Pavlovsky's experiments.

Sexual isolation can thus be produced by mating preferences in favour of two or more different genotypes. This is the sexual equivalent of disruptive natural selection in which different genotypes are favoured in different environments. When this occurs, the hybrids may indeed be disadvantageous, being adapted to none of the environments as well as each particular strain. This disruptive natural selection will thus allow the evolution of mating preferences in each strain, and therefore produce what may be called disruptive sexual selection.

ENZYMES

Orbital Argument

from our Molecular Biology Correspondent

SOME months ago I described what seemed at the time the obliteration by Bruice and his colleagues of Koshland's "orbital steering" theory of enzymatic catalysis. Those people who enjoy the cathartic effects of an intellectual punch-up will be delighted to see that Koshland has not taken the assault on his brainchild lying down, and has come storming back in the current issue of the *Proceedings of the US National Academy of Sciences* (Dafforn and Koshland, *Proc. US Nat. Acad. Sci.*, **68**, 2463 ; 1971).

The argument really hinges on how close must be the angular restriction on the line of attack of one reactant by another in order to bring about a rate enhancement of a good many orders of magnitude. Bruice *et al.* concluded from some very straightforward calculations of orientation factors that large enhancements demand an angular precision of the order of 0.1°, which would fall within the range of normal vibrations. Dafforn and Koshland criticize the logic which leads to this conclusion, first of all on the grounds that the orientation of only one of the reactants was considered, and secondly that the calculation pertains to a substantially higher rate increase than it is necessary to find, given that there is some choice in distributing rate-enhancement factors between different possible causes. Adjustments for these considerations, say Dafforn and Koshland, bring the angular restriction up to the altogether more reasonable level of 10°—though this is still not very different from room-temperature vibrations. They go on to show that if one computes the entropic effect of rotational immobilization of the reactants, that is to say one locks them in a favourable orientation for attack, one can come by an adequate enhancement factor. They also then calculate the change in the energy of the transition state, corresponding to a given change in the angle of approach, using a simple harmonic oscillator model with a reasonable value for the bending force constant. Depending on the force constant chosen, the rate factor falls off fairly rapidly with angular distortion.

What then are we to believe? It is clearly possible for theoreticians to hurl formulae at each other, which prove their opposing cases with comparable conviction, and presumably to their entire satisfaction. It is perhaps not unfair to take the view that the onus of persuasion is on Koshland, because his notion does represent a departure from implicit chemical thinking. His classical calculations inevitably make several considerable numerical assumptions about the nature of the transition state. Moreover, there are the quantum mechanical calculations of Port and Richards to be considered (*Nature*, **231**, 312 ; 1971).

Storm and Koshland, in their original formulation of the "orbital steering" concept, gave as evidence in its favour the relative rates of intramolecular esterification in a set of compounds in which the reacting carboxyl and hydroxyl groups were positioned with different degrees of rigidity, and also the relative rate of thioester formation when sulphur was present in place of oxygen. Port and Richards have simply calculated the overlap integrals for the orbitals involved in the reaction, on the grounds that these must be expected to reflect the relative reaction rates, if the orientation factor is indeed dominant. As one might intuitively expect for the set of components, on the grounds of the diffuseness of molecular orbitals, the variation in overlap integrals is slight. Port and Richards concede that more refined calculations would be both possible and desirable, but their results as far as they go certainly argue against the importance of the critical angular orientation factor.

At the very least then one may say that Koshland's case is not proven, though of course the strategy of destruction is always much the easier in such a situation. In Koshland's favour it might be argued that orbital steering should not be discarded until a good alternative can be found, and Koshland rejects the proximity effect (that is the translational, as opposed to rotational immobilization of the reactants, in juxtaposition at the active site) as a

Defective Mouse Sarcoma Virus

As RNA tumour virologists learn progressively more about the biology of the mammalian and in particular mouse sarcoma and leukaemia viruses, it is becoming increasingly apparent that these viruses are capable of essentially the same range of interactions with their host cells as their avian counterparts, the Rous sarcoma viruses and avian leukosis viruses. In *Nature New Biology* next Wednesday, for example, Gazdar, Phillips, Sarma, Peebles and Chopra describe the isolation and properties of a noninfectious mouse sarcoma virus which is reminiscent of the noninfectious Rous sarcoma viruses produced by certain chick cells transformed by Bryan high titre Rous sarcoma virus in the absence of an avian leukosis helper virus.

Gazdar *et al.* noticed that two lines of hamster cells derived from sarcomas induced in hamsters by mouse sarcoma virus liberated typical C-type virus particles with all the biophysical parameters of the sarcoma leukaemia viruses. These virus particles, in spite of the fact that they are liberated from hamster cells, proved to cross react with antisera against the mouse sarcoma and leukaemia viruses but failed to cross react with antisera directed against hamster leukaemia viruses. In short, the virus liberated by the hamster cells is antigenically related to mouse, not hamster, C-type viruses.

Is the virus from the hamster cells infectious? All the attempts which Gazdar and his colleagues have made to transform mouse rate and hamster cells growing in a variety of culture conditions have failed and neither does the virus induce sarcomas or leukaemias when injected into newborn rats, mice or hamsters. Gazdar *et al.* were, however, able to prove that these apparently noninfectious mouse C-type virus particles do indeed contain that part of the mouse sarcoma virus genome which is responsible for transformation and sarcomagenesis by sedimenting this virus with mouse leukaemia virus. During such co-sedimentation the two viruses are presumably physically fused together, for the pelleted virus particles will transform cells and at low efficiencies induce sarcomas. After sedimentation alone neither the noninfectious sarcoma virus nor the leukaemia virus has these properties.

Gazdar and his colleagues conclude that the virus which they have isolated from these hamster cells contains the mouse sarcoma virus genome but lacks helper leukaemia virus of either mouse or hamster origin. The parallels and differences between this virus, another defective mouse sarcoma virus isolated recently by the same group (*Proc. US Nat. Acad. Sci.*, **68**, 1520 ; 1971), and the defective Rous sarcoma viruses discovered and studied by Weiss and the Hanafusas deserve and are no doubt receiving further attention.

candidate in quantitative terms. On the simplest argument, based only on translational entropy, the proximity factor on the reaction rate should be only a matter of 55. Page and Jencks (*Proc. US Nat. Acad. Sci.*, **68**, 1678 ; 1971) have now argued, on the basis of calculations of translational and rotational entropy changes on binding the reactants, that the effect may be very much greater, and that effective reactant concentrations of 10^8 molar can be achieved at an active site. On this view, the enzyme operates primarily as an entropy annihilation machine to produce the required rate enhancement. Dafforn and Koshland take issue with Page and Jencks, and trade approximation for approximation, and entropy unit for entropy unit. They also make short work of Reuben's argument (*ibid.*, 563) regarding the longer sticking time of reactants on the active site, compared with free solution collisions, by pointing out that this is compensated by a correspondingly lower collisional frequency.

The argument will clearly continue, and the difference of view between Koshland and Jencks will readily lend itself to semantic hair-splitting. Whether or not orbital steering is now a dead duck is a matter on which most enzymologists will make up their own minds. There is no doubt, however, that it has sparked off an uncommonly interesting argument.

GENE EXPRESSION

Modifying Transcriptase

from our Cell Biology Correspondent

NOT so long ago when sigma factors were at the height of fashion they were being invoked whenever questions of the regulation of gene expression were being discussed. The simple notion that core DNA dependent RNA polymerase (α_2,β,β'), a nonspecific machine for catalysing the polymerization of ribonucleoside triphosphates into RNA, might specifically be programmed by a set of different sigma factors each of which restricted transcription to a particular set of genes could be adapted to explain almost any pattern of regulated gene expression. This idea has, however, lost much of its appeal, not least because the putative sets of sigma factors have not materialized. Indeed, in perhaps the most intensively investigated system in which there is a regulated change in the pattern of transcription—the replication of phage T4 in *Escherichia coli*—it is modifications of the polypeptide chains which comprise the cell's core enzyme and factors involved in termination that seem to play a crucial part in switching transcription on and off.

As Schachner and Zillig report (*Europ. J. Biochem.*, **22**, 513 ; 1971), the core DNA dependent RNA polymerase which is isolated from *E. coli* some 10 minutes after infection with T4 differs in all its subunits from the core enzyme of uninfected cells. Fingerprints of tryptic peptides from modified (post-infection) and unmodified (pre-infection) core enzyme reveal the following: after infection the α chain of the core enzyme apparently gains additional amino-acids and, as Goff and Weber have reported, an adenylic acid residue ; the β' chain is modified such that it yields on tryptic digestion an additional tyrosine containing peptide and one of the histidine containing peptides has an altered mobility ; finally, the β chain from modified core yields a significantly different set of histidine and tryptophan containing peptides.

In short, every polypeptide chain in the core enzyme is altered after T4 infection and Schachner *et al.* (*ibid.*, 520) attempted to correlate these changes with changes in the pattern of transcription of the T4 genome. The chief events are, first, the switching off of host RNA and protein synthesis, which occurs in the absence of protein synthesis and can be brought about by allowing phage ghosts to adsorb to the cells. Once this step has occurred the immediate early genes, then the delayed early genes and finally, after DNA replication, the late genes of the phage are transcribed. This regulation is not the result of the sequential modifications of the three species of polypeptide chains in the core enzyme, for within 4 minutes of infection, before delayed early and late RNAs appear, all three chains have been modified. Modifica-

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From T$_4$ to Man

WHEN Alberts and Frey (*Nature*, **227**, 1313 ; 1970) described the properties of the gene-32 protein in T$_4$ bacteriophage it was hailed as a milestone in the understanding of both genetic recombination and DNA synthesis. Hotta and Stern (in next Wednesday's *Nature New Biology*) now announce that proteins with very similar properties to that of this T$_4$ protein can be isolated from spermatocytes of three mammalian species, namely rat, bull and man. Evidence that meiotic cells of lily contain this DNA-binding protein has already emanated from Hotta and Stern's laboratory (*J. Cell Biol.*, **47**, 91a ; 1970), so that it seems highly likely that the protein may occur universally.

On the basis of various bits of information which have become available over the past couple of years, Hotta and Stern have pieced together their model for recombination. The picture which is emerging is of two types of pairing during meiosis, one occurring at zygonema and resulting from delayed replication of small stretches of DNA such that only short segments of the chromosome are paired; this would be most likely coordinated with synaptonemal complex formation and the stabilization of the chromosome pairs. It is suggested that the second type of pairing would follow this initial alignment, with nuclease and other enzymes producing single stranded regions of DNA. The type of recombination which other authors have described might then occur within these regions. Hotta and Stern think that the DNA-binding protein may play some part in either of these two forms of association but because of the widespread distribution of the protein it seems likely to be of important functional significance for meiosis generally.

The protein was isolated from meiotic prophase nuclei, assaying for DNA-binding activity in much the same way as Alberts's T$_4$ protein and comparing the activity with that of the other spermatocyte nuclei. On fractionation, the greatest amount of the mammalian DNA-binding protein was found in exactly the same band as that in which the lily DNA-binding protein is found and, more important, the properties of all proteins, T$_4$, lily and the mammalian ones, seem to be identical.

All of the DNA-binding proteins are capable of renaturing denatured, single stranded DNA at a very fast rate and all of them will bind very similar amounts of DNA. Thus, in spite of the very limited purification which centrifugation achieves, the ratio of DNA bound to protein is approximately the same in all instances and suggests that the proteins have very similar DNA binding capacities.

Moreover, the elution profiles from both DEAE cellulose and from DNA columns have almost identical patterns, so that it would seem that the protein is a distinctive and general feature of eucaryotic nuclei. Because Hotta and Stern only find appreciable quantities of the protein in prophase nuclei with the other spermatophyte nuclei and the nuclei of somatic tissues containing insignificant amounts, it is not unreasonable to assume that the protein plays an important part in some facet of meiosis, and in view of the T$_4$ evidence, neither is it unreasonable to suppose that it has some recombinogenic activity.

This is interesting information and no doubt the next step in the confirmation of the protein's role will come from a determination of whether cells which undergo induced somatic recombination have elevated levels of the protein.

tion of core enzyme thus seems to be a very early event in T4 replication.

What then causes the switch from immediate to delayed early gene transcription and later to late gene transcription? From comparisons of the pattern of phage RNA made *in vivo* in the presence and absence of protein synthesis and the presence or absence of phage DNA replication (replication is blocked with certain mutant phage) and the ability of cell extracts to make RNA *in vitro* Schachner *et al.* suggest that one of the proteins specified by the immediate early genes is an anti-terminator factor which allows RNA polymerase to read through from the immediate early to the delayed early genes. Similarly, in the absence of DNA replication immediate early and delayed early RNA, but no late RNA, is made, and again Schachner *et al.* interpret this in terms of failure in normal termination, rather than initiation mechanisms, which stocks up the enzyme at the end of the delayed early genes. In short, regulation of termination may be at least as important as regulation of initiation in this particular example of controlled gene expression.

REMOTE SENSING

Using ERT Satellites

from a Correspondent

INTEREST in the potential of remote sensing techniques has been slow to develop among field scientists in the United Kingdom compared with their colleagues in North America. This can very largely be explained by the relatively high cost of remote sensing operations, the scarcity of suitable sensors in the UK, the geometric limitations of many existing sensors and also a general lack of understanding of present capabilities. The offer, made throughout the world by NASA last year, of an opportunity to participate in its forthcoming series of Earth resources technology satellites has eliminated many of these reasons. NASA has undertaken to provide both a free platform, the ERT satellites, and free imagery on film and/or digital tape to all research workers who submit acceptable proposals. NASA will carry out digitization and geometric correction of the imagery at its ground data processing facility.

It was with the aim of stimulating an exchange of ideas on the subject of remote sensing, with particular reference to Earth resources satellites, that a small group of interested scientists and technologists met for an afternoon seminar in Imperial College, London, on October 22. Professor P. A. Sheppard (Imperial College), chairman of the Space Committee of the Royal Society, presided over the session.

Dr Norman Simmons (Ministry of Defence) opened the meeting with a presentation on the state-of-the-art in remote sensing from space. Dr Simmons was particularly concerned to point out the limitations in the resolution of existing systems and the likely extent of possible improvements. At present a ground resolution of 50 m can be considered better than average and the systems fall rather short of the resolutions demanded by topographic mapping. Dr D. Parry (Hunting Surveys) followed with a description of an analysis of an oblique, hand-held photograph from Gemini VI of part of West Pakistan. Field surveyors had already worked in the area, mapping vegetation, soils and land use. By following a systematic procedure of tonal classification, pattern interpretation, collation of information available before field work and a subsequent comparison of these maps, Parry was able to demonstrate that, had the field surveys been presented with the photography beforehand, they could have significantly reduced the density of field sampling. This was in spite of considerable blurr, a varying scale in the perspective view and a predominantly blue coloration in the film.

Dr J. A. Jones (Experimental Cartography Unit, Royal College of Art) then spoke about plans to analyse the mappable content of ERTS-A imagery by computerized comparison between the imagery and previously mapped "ground truth" data on vegetation, geology, land use, soils and topography. The "ground truth" data consist of digitized field maps, that is, strips of identification codes and coordinates filed on magnetic tapes, and are the raw material for current experiments in structuring a computer storage and retrieval system for cartographic information. The experiment is centred on the Upper Thames Valley.

Dr J. Norman (Imperial College, London) attempted to forecast the value of ERTS imagery for geological pur-

The Tasman Geosyncline and Global Tectonics

THE long process of reinterpreting known geological regions in terms of the modern concepts of seafloor spreading and plate tectonics takes a further step forward with the publication of Oversby's analysis of the Tasman Geosyncline in next Monday's *Nature Physical Science*. This is not the first time that the concepts of the new global tectonics have been successfully applied to orogenic belts, for last year Bird and Dewey (*Bull. Geol. Soc. Amer.*, **81**, 1031 ; 1970) analysed the evolution of the Appalachian orogen in terms of lithospheric plate-continental margin tectonics and published a major article on the more general question of mountain building (*J. Geophys. Res.*, **75**, 2625 ; 1970). Because mountain building has been a central and fundamentally insoluble problem in geology since the early days of the subject, the second article marked a significant victory for the new global tectonics and proof that it may be successfully applied in a more detailed form than the simple conceptual model.

Oversby's analysis—the first for the Tasman Geosyncline—also illustrates the applicability of the new global tectonics in detail—detail which cannot be summarized in a few paragraphs. In general terms, however, Oversby envisages the action of several tectonic cycles during the late Precambrian and Palaeozoic evolution of the southern part of the Tasman Geosyncline. For each cycle there was a time lag between the start of plate motion and its first effects on the continental side of the trench complex of which the geosyncline now forms a part, and a similar lag between the cessation of motion and the final effects. On the other hand, the effects of each successive cycle probably overlapped those of the previous cycle temporally and geographically.

Other conclusions reached by Oversby are that the westward motion of the downwelling oceanic plate was probably slow and that the downwelling (consuming) plate margin seems to have migrated eastwards. The first conclusion is supported by the "relatively mild tectonism spread over a period of time, which does not seem to have produced very marked topographic relief" and the second by the eastward younging of plutonics. The absence of major topographic highs at any time would also explain the marked lack of gravity slide sheets in the Tasman Geosyncline and, combined with the slow eastward migration of the margin, could explain the predominant presence of steep structures—in short, the usual effects of plate interaction seem to have been mitigated.

In attempting to relate the known geology of the Tasman Geosyncline to plate tectonics, Oversby admits that his interpretation may not be universally accepted. His admitted aim, however, is to provoke discussion. In the sense that the concepts of plate tectonics will ultimately be accepted or rejected on the basis of their application or non-application in detailed situations, the discussion must be important.

poses. The chief areas seem to be in the location of large scale structures in sedimentary rocks which might form oil traps, detection of ore bodies in arid areas, in engineering geology and in detecting major regional fractures. In discussing possible applications, Dr D. E. Pedgley (Centre for Overseas Pest Research) described the need for regular coverage of potential breeding grounds for the desert locust in parts of the Middle East. The search is aimed at detecting areas of recent rainfall, where the females can lay their eggs. Finally, Dr W. T. Welford (Imperial College, London) gave a brief outline of the potential of an optical Fourier transform instrument for use on ERTS imagery. This presents particular problems because of the high density of scan lines in the return beam vidicon output (4,200 on 70 mm format).

ACETYLCHOLINE RECEPTORS

After Denervation

from our Neurochemistry Correspondent

A PROBLEM of interest to neurobiologists for some time has been that of the development of neural connexions. Many approaches, involving a variety of techniques, have been used in this rather diffuse field of study, but one of the more successful has been the observation of changes in neuromuscular synapses in developing animals, and in mature animals after the normal nerve supply to muscles has been interrupted.

Transmission at a mature vertebrate neuromuscular junction occurs by the release from nerve terminals, in response to the arrival of nerve impulses, of discrete quantities of a chemical mediator, acetylcholine (ACh), which interacts with specific receptors on the muscle surface, thereby causing a characteristic permeability change, which excites the muscle membrane. Sensitivity to ACh is normally restricted to small "end-plate" regions, where the nerve endings make contact with the muscle, but if a muscle is deprived of its nerve supply it becomes responsive to ACh along the entire length of its surface. Foetal muscle fibres are similarly uniformly sensitive to ACh, and only after birth is there a retraction of sensitivity to the limited area of contact with the nerve; this occurs in parallel with the development of the characteristic end-plate structure. Reinnervation of a denervated muscle in a mature animal can also effect a similar shrinkage of ACh sensitivity; it seems therefore that this selection process requires some sort of neural influence.

Localization of ACh sensitivity in intact muscles is not entirely precise—some extra-junctional responses have been obtained, especially at the ends of fibres, where they fuse with tendons, but the sensitivity of ACh at these sites is considerably less than at the end-plate itself. Until comparatively recently it was assumed that the responses to ACh of both junctional and extra-junctional sites were more or less analogous, but in two articles in the current issue of the *Journal of Physiology* (**218**, 85 and 101; 1971), Anne Feltz and Alberto Mallart suggest that qualitative differences may exist between them.

Feltz and Mallart studied responses to ACh by iontophoretic application together with intracellular recording from muscle fibres. The characteristic end-plate responses showed a high sensitivity to ACh, with a rapid rise time independent of the dose of ACh applied. By contrast, the sensitivity to ACh at extra-junctional sites was lower, and responses had a longer rise time, which increased with increasing doses of ACh.

Transmitter action at the neuromuscular junction normally causes a local fall in the membrane potential, which in turn triggers impulses in adjacent areas of membrane. By displacing the membrane potential artificially and measuring the resultant change in the size of the ACh-induced depolarization (end-plate potential or e.p.p.), it has been found that the null point for the e.p.p. is -10 to -20 mV;

Pulsars and Supernova Remnants

RECENT observations of the Vela pulsar (PSR 0833–45), which was the first pulsar seen to glitch, and CP 1919, the first pulsar to be identified, provide new clues to the nature and origin of these objects. In next Monday's *Nature Physical Science*, P. E. Reichley and G. S. Downs, of the Jet Propulsion Laboratory, CalTech, report a discontinuous change of period in the Vela pulsar between August 24 and September 4, 1971. The previous recorded glitch in this source took place between February 24 and March 3, 1969. The interval between glitches fits well with the planetary perturbation model proposed by C. Michel, in which the close approach of a planet in a highly eccentric orbit produces a tidal starquake. But other theories remain viable, and perhaps the most significant aspect of the discovery of glitches in this pulsar is that it necessitates the revision of age estimates upwards, making it more likely that the pulsar is indeed as old as the Vela X supernova remnant which surrounds it.

Also in next Monday's *Nature Physical Science* are two independent reports concerning the non-thermal shell source close to CP 1919 in the sky. This is the source reported last year by Caswell and Goss (*Astrophys. Lett.*, **7**, 141; 1970). W. M. Goss and U. J. Schwarz have now carried out a further survey of this part of the sky using the Westerbork array. They have found that the source has a shell structure, with the pulsar lying at the edge of the shell. The shell source itself is rather weaker than a typical supernova remnant (SNR), but comparisons are somewhat misleading because there is no such thing as a typical SNR.

Superficially, there are severe problems in identifying the shell source as an SNR associated with the pulsar CP 1919. The age of the pulsar is estimated as 10^7 yr, that of the shell source as 5×10^4 yr. The pulsar is widely believed to be at a distance of no more than 650 pc from Earth, yet the shell source is, if an SNR, at roughly 7 kpc. But the theoretical model for the origin of pulsars in supernova explosions is so strong, and the chance of finding a pulsar and an SNR aligned on the sky is so small, that these problems might be resolved.

In the same issue of *Nature Physical Science*, M. R. Kundu and T. Velusamy agree with the suggestion of Goss and Schwarz that a runaway pulsar could plausibly have reached the edge of the associated SNR since its formation. The more detailed analysis of Goss and Schwarz also suggests solutions to the other difficulties. The pulsar could be at the distance implied by taking the shell source to be an SNR, if the electron density in the line of sight to it is unusually low. In this case, the age difference could be resolved if CP 1919 is the older member of a binary pair, and the SNR results from the explosion of its companion comparatively recently. This would also allow plenty of time for the separation of the two components since the supernova in which CP 1919 formed, and it is not surprising, on the highly directional rotating neutron star model, that the younger associated pulsar cannot be seen.

Even more attractive is the possibility that the shell source is at 250 to 650 pc. In this case, it would represent a new type of galactic object, much weaker than an SNR, created either from the recent birth of the pulsar with a relatively long period of $\sim$1 s from a star only marginally suitable to evolve into a neutron star, or, perhaps, from a second event later in the history of a more typical pulsar.

beyond this level ACh causes a potential change in the reverse direction from the normal. The "reversal" potential for the action of a particular drug or transmitter depends on the changes in the ionic permeability of the membrane produced by the interaction of the drug with its receptors. These changes can be deduced from the effect of altered ionic media on the position of the null point; in the case of ACh acting at the end-plate, the permeability to sodium and potassium ions only is increased by the transmitter.

In their second article, Feltz and Mallart describe experiments in which they used similar techniques to determine whether the same permeability changes are produced by the action of ACh at the extra-junctional receptors of normal frog muscles and at those induced by denervation. The results showed that although responses at both these types of receptors are also mediated exclusively by changes in cationic permeability, they have a reversal potential which is substantially more negative (−40 to −50 mV) than that observed at the normal neuromuscular junction.

The most rational explanation for this is that, during junctional and non-junctional responses, the permeabilities to sodium and potassium are altered relative to each other in a different fashion, thus indicating a real difference in ionic selectivity between junctional and non-junctional receptors. This selectivity could be caused by an altered association outside the end-plate between receptors and ion channels which have been opened up during their activation ("ionophores"), or by a genuine difference in the receptors themselves. Pharmacological studies have indicated that the ACh receptors which are induced after denervation are less sensitive to curare (Beranek and Vyskocil, *J. Physiol.*, **188**, 53; 1967), and of interest also are the recent experiments of Miledi and Potter (*Nature*, **233**, 599; 1971) on the binding of α-bungarotoxin to muscles. These studies suggest that two different classes of ACh receptor may exist at the end-plate itself, one of which has a low affinity for curare, and might therefore be analogous to the "slow-rise-time", "more-negative-reversal-potential" receptors of Feltz and Mallart. The toxin also binds to receptors induced after denervation, and its use will, no doubt, make possible their isolation and characterization, as well as that of the junctional and extra-junctional receptors of normal muscle. In the meantime, however, the discovery of measurable differences in the responses of these classes of receptor must stimulate further study of the influences which determine their formation.

PLANT PHYSIOLOGY

Phloem Transport

from a Correspondent

IT may seem surprising that after more than forty years of intensive study by some of the most able plant physiologists of the day, the mechanism whereby organic substances, notably sugars, are transported in the phloem of plants is still unknown. The reason why this problem is unsolved is not hard to find. Transport occurs through narrow pipes—the sieve tubes—which, unlike the xylem vessels through which water moves, are alive and very sensitive to disturbance which readily leads to loss of function. Moreover, normal transport occurs only when the sieve tubes are connected at their ends with living cells which supply and receive the transported materials and there are some indications that association with living cells along the conducting strand is also essential. With such a complex multi-cellular system it is very difficult to obtain experimental results which can be interpreted unequivocally. Phloem transport is therefore an ideal subject for lively discussion, as was shown at a meeting organized by the Physiochemical and Biophysical Panel of the Society of Chemical Industry held in London on October 18 under the chairmanship of Professor P. E. Weatherley.

The most widely supported mechanism is still the one advocated in 1930 by the German botanist, Münch, and now usually referred to as "pressure flow". According to this hypothesis, movement of sugar into a sieve tube at one end (the source) and its removal at the other (the "sink") causes, by osmosis, a difference in hydrostatic pressure between the two ends and leads to a mass flow of water and dissolved substances along the tube.

A major drawback to the pressure flow hypothesis, as was pointed out at the meeting by Dr D. C. Spanner (Bedford College, London), is that if there are obstacles in the sieve tube lumen which significantly increase its resistance to linear flow, the pressure gradient required to force liquid through the tube at the rate observed would be much greater than that which is likely to occur. Both light and electron microscopic evidence suggests that such obstructions in the form of protein fibrils ("P protein") occur both in the lumen of the sieve tube and in the pores of the perforated baffles (sieve plates) which occur at frequent intervals along its length. Unfortunately the evidence from microscopic studies does not unequivocally establish the condition of the sieve tube in the normal functional condition and proponents of the pressure flow hypothesis contend that the apparent blocking of sieve tube lumen and sieve plate pores with P protein is an artefact arising from the release of pressure which occurs when the material is being prepared for microscopic observation.

Spanner rejects this argument (*Nature*, **232**, 157; 1971) and believes that the pressure flow mechanism is untenable because of the impossibly high pressure gradients which would be required to force liquid through partly obstructed tubes. He has suggested that mass flow through the sieve tubes is brought about by an electro-osmotic mechanism operating across the sieve plate. Thus the sieve plates have a vital role in boosting flow at intervals along the transport pathways instead of being a hindrance as they are to the pressure flow mechanism.

The electro-osmotic mechanism was criticized by Dr E. A. C. MacRobbie (University of Cambridge) on the grounds that the fluxes of potassium ions required to maintain the necessary electrical gradient across the sieve plate in the manner proposed by Spanner would be several orders of magnitude greater than those normally found in living cells, and would be beyond the energetic capability of the cells concerned. She put forward an alternative hypothesis similar to that recently advocated by a Cambridge colleague, F. B. P. Wooding. Wooding has proposed (*Phloem* (Oxford Biology Readers, No. 15); Oxford University Press, 1971) that longitudinal movement of solution in the sieve tubes may be brought about by rhythmic undulations of P protein fibrils. Contraction and relaxation of protein fibres have already been implicated in the circulation of cytoplasm in some algal cells and in fungal filaments. There is some evidence that P protein fibres can be induced to contract by ATP in the same way as muscle fibres and flagellae, but further biochemical studies of P protein fibres are required before much credence can be given to this hypothesis.

The contractile fibre mechanism has a good deal in common with the proposal of R. Thaine that transport in sieve tubes occurs through "transcellular strands" by peristaltic pumping caused by contraction and relaxation of protein constituents in the walls of these strands. Dr Thaine was unable to be present at the meeting but Dr D. Aikman (University of East Anglia) presented some calculations which indicate that this mechanism is energetically quite feasible. In spite of the recent observations of Jarvis and Thaine (*Nature New Biology*, **232**, 236; 1971) most plant physiologists remain sceptical about the reality of transcellular strands. Elucidation of the structure of functional sieve tubes is required before any one of the current hypotheses can be supported.

Origins and Evolution of Ornithischian Dinosaurs

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Recent discoveries in the red beds of the Upper Trias have shed light on the history of the ornithischian dinosaurs. It is suggested that these dinosaurs had a monophyletic origin among advanced pseudosuchian thecodonts. Development of their rather bird-like pelvis involved backwards rotation of the pubis and subsequent growth of a prepubis. A conservative stock of primitive-looking hypsilophodonts, which persisted from the late Trias through the Cretaceous, lay at the core of ornithischian phylogeny.

BOTH orders of dinosaurs, Saurischia and Ornithischia, came into existence during the Triassic period. The study of saurischian phylogeny is a fairly straightforward matter since there is a wealth of information on Triassic forms[1-3]. Early ornithischian history, in contrast, is obscure. Before 1962 the genus *Geranosaurus*, which is represented by a single jaw[4], was the only undisputed Triassic ornithischian on record, but since that date knowledge of the earliest ornithischian dinosaurs has increased considerably; Upper Triassic forms have been discovered in southern Africa[5-8], China[9], Argentina[10], Nova Scotia[11] and, possibly, in Europe (my work in progress). This accumulation of new evidence permits critical reappraisal of ornithischian origins and evolution.

Monophyletic Origin

Recent discoveries show that the ornithischian dinosaurs had an almost worldwide distribution as early as the Upper Trias. Such a geographic range implies that ornithischian history extends well back into the Triassic period (that is to say, there must have been some considerable episode of dispersal before the Upper Trias). Ewer[12] has reiterated Broom's suggestion[13] that Lower Triassic pseudosuchians such as *Euparkeria* are close to the ancestors of the Ornithischia. Unfortunately, none of these pseudosuchian reptiles shows any obvious tendency towards the ornithischian state of organization. The pseudosuchians and the ornithischians would seem, in fact, to be quite irreconcilable in terms of pelvis and ankle structure (Figs. 2 and 3). In the pseudosuchian pelvis (Fig. 2*A*) the pubis is directed anteroventrally; in the typical ornithischian pelvis (Fig. 2*C*) this bone consists of two branches—one (prepubis) extends forwards and the other (postpubis) runs down and back against the ischium. At first glance it seems unlikely that the ornithischian pelvis could have been derived from the pseudosuchian type of pelvis, but the pelvic bones of *Fabrosaurus*, an ornithischian dinosaur from the African Trias, indicate how such derivation might have occurred. In *Fabrosaurus* (Fig. 2*B*) the rod-like postpubis is developed in typical ornithischian

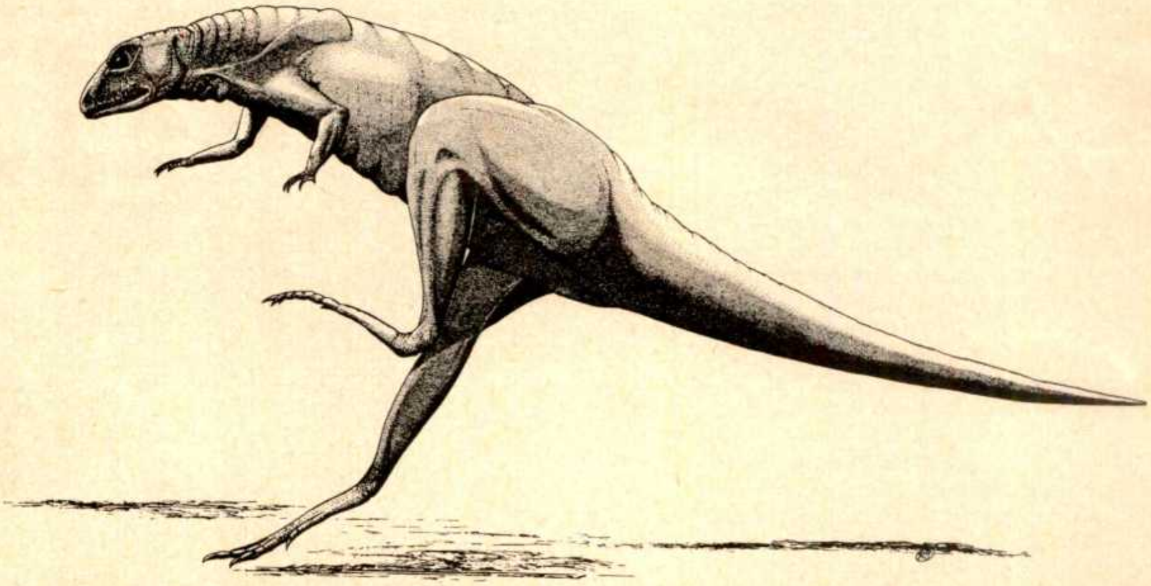

Fig. 1 Flesh restoration of the primitive ornithischian dinosaur *Fabrosaurus*, based on remains from the Upper Trias of southern Africa. This herbivorous dinosaur was about a yard long and was well adapted for fast bipedal running. Similar animals persisted until the close of the Cretaceous and probably represent the basal stock of the ornithischian dinosaurs.

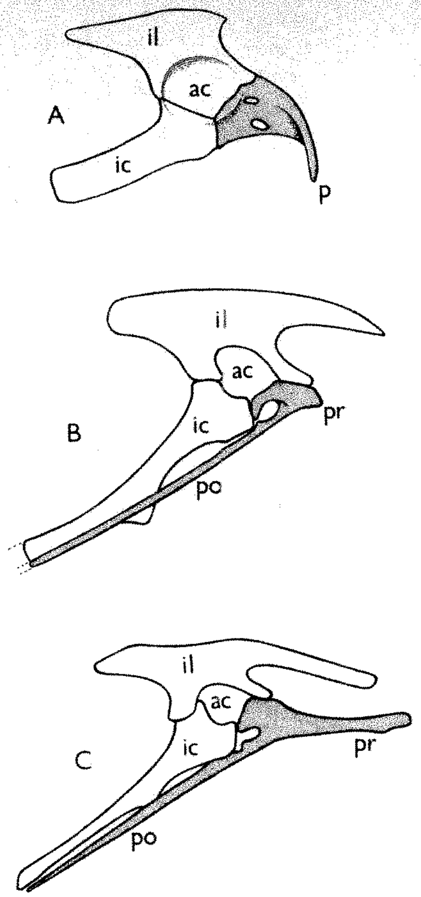

Fig. 2 Comparative diagrams of the pelvis in the pseudosuchian *Euparkeria* (*A*), the Triassic ornithischian *Fabrosaurus* (*B*) and the Cretaceous ornithischian *Thescelosaurus* (*C*). In each case the pelvis is viewed from the right side and the pubic bone is emphasized by shading. *ac*, Acetabulum; *ic*, ischium; *il*, ilium; *p*, pubis; *po*, postpubis; *pr*, prepubis. Diagrams *A* and *C* after Romer[19].

fashion, but the incipient prepubis is merely a short stump of bone. This remarkable pelvic structure suggests that the ornithischian postpubis is homologous with the pubis in other reptile groups and that the prepubis is a neomorphic feature. Hence the pseudosuchian/ornithischian transition would have involved a backwards rotation of the pubis (to form the postpubis) and the subsequent development of a prepubis. Such a transition would also require a number of relatively minor changes, notably perforation of the acetabulum and extension of the ilium to form a salient anterior process. It may be concluded that the pseudosuchian and ornithischian types of pelvis are not totally irreconcilable in structure and that the latter may have arisen from the former.

But the origin of the ornithischian ankle joint still presents a formidable problem. In the ankle of *Euparkeria* (Fig. 3*A*), the astragalus is simply an extension of the tibia and the calcaneum forms a heel-like adjunct to the foot. In this rather complex tarsal system the "hinge" of the ankle separates the calcaneum from the astragalus. The ornithischian ankle (Fig. 3*B*) displays a somewhat simpler mesotarsal joint and the "hinge" of the ankle runs transversely beneath the astragalus and the calcaneum. The mesotarsal joint is in evidence as early as the Upper Trias (in the South American *Pisanosaurus*[10]) and cannot be envisaged as a simple modification of the pseudosuchian ankle joint. So it is clear that the ancestors of the Ornithischia must have differed from *Euparkeria* in ankle construction.

Although it may be deduced that the ornithischians arose from pseudosuchian reptiles which are at present unknown, this still does not clarify the problem of ornithischian history during the Trias. The apparent hiatus between advanced pseudosuchians and early ornithischians arises chiefly from a deficient knowledge of terrestrial reptile faunas during the Middle Trias. There are, in consequence, no "intermediates" between the Lower Triassic pseudosuchians and the earliest known (Upper Triassic) ornithischians.

In spite of the obscurity surrounding early ornithischian history it is possible to infer, with a fair degree of certainty, that the ornithischian dinosaurs had a monophyletic origin and that the order Ornithischia is a "natural group". Such an inference is supported by several independent lines of reasoning. First, it is probable that the varied ornithischian types of the Jurassic and Cretaceous (iguanodonts, hadrosaurs, ceratopsians and the like) arose from ancestors within a single family, the Hypsilophodontidae. This basic assumption is sustained by the observation that advanced ornithischians (most particularly the iguanodonts and the hadrosaurs) may be derived from hypothetical hypsilophodont ancestors. This much, at least, of ornithischian history is fairly clear and has been adequately expressed by Romer[14]. Second, it transpires that all well known Triassic ornithischians are hypsilophodonts. These early dinosaurs display certain features (for example, toothed premaxillae, tibiae longer than femora) which are characteristic of the family Hypsilophodontidae. This evidence endorses the suggestion that the hypsilophodonts are at the core of ornithischian history. Finally, there is a remarkable homogeneity of structure throughout the order Ornithischia. Singular and diagnostic features, such as the biramous pubis and the predentary bone (at the mandibular symphysis), are encountered in even the most aberrant ornithischians. It seems unlikely that structures as peculiar as these could have been developed in more than a single group of advanced pseudosuchians. All of these inferences point to a monophyletic origin for the order Ornithischia and emphasize the fundamental role of the hypsilophodonts in ornithischian phylogeny.

A Hypsilophodont Plexus

The earliest known ornithischians are therefore Upper Triassic representatives of the family Hypsilophodontidae. These Triassic hypsilophodonts may be divided, on the basis of cranial and dental characters, into two quite distinct groups. One group, exemplified by the African *Lycorhinus* (*Heterodontosaurus*)[5,8], may conveniently be termed the lycorhinids; these have, as one of their peculiarities, large canine-like teeth in both upper and lower jaws. The functional significance of these teeth is debatable, especially since the lycorhinids seem, like all other ornithischians, to have been herbivorous. It is possible that the canines were used as defensive weapons or that they expressed sex dimorphism, but there is no real evidence for either of these theories. *Geranosaurus*[4], also from the African Trias, has

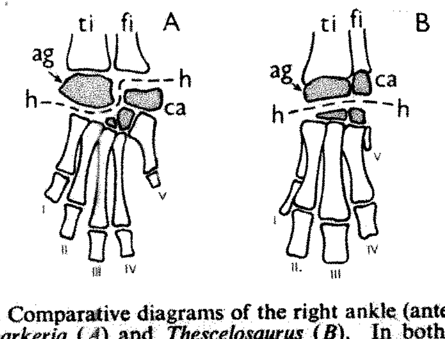

Fig. 3 Comparative diagrams of the right ankle (anterior view) in *Euparkeria* (*A*) and *Thescelosaurus* (*B*). In both cases the tarsal bones are shaded. *ag*, Astragalus; *ca*, calcaneum; *fi*, fibula; *h*, line of "hinge" through ankle; *ti*, tibia. Both diagrams after Romer[19].

traces of an enlarged (canine?) tooth and might be regarded as an ally of *Lycorhinus*. Apart from this dental peculiarity the lycorhinids are further distinguished by having a deep longitudinal recess in the exterior of the maxilla and by the absence of teeth from the front of the premaxilla.

The other Triassic hypsilophodonts, best represented by the African genus *Fabrosaurus*[6,7], may be grouped together as the fabrosaurs. The fabrosaur dentition lacks any canines; the premaxillary teeth extend to the tip of the snout and the lateral face of the maxilla is almost flat. These distinctions between the fabrosaurs and lycorhinids (so striking that Romer[14] accords the lycorhinids separate familial status) evidently reflect some evolutionary dichotomy of the ornithischian dinosaurs before the Upper Trias. This remarkably early episode of ornithischian diversification had never been surmised. The lycorhinids seem to have been restricted to southern Africa, whereas the fabrosaurs are found as far afield as China (*Tatisaurus*[9]) and South America (*Pisanosaurus*[10]). It is also significant that the lycorhinids seem to have no post-Triassic derivatives whereas the fabrosaurs may be regarded as forerunners of the Jurassic and Cretaceous hypsilophodonts. Hence the fabrosaurs represent the earliest known portion of a hypsilophodont stock which persisted until the end of the Cretaceous. The lycorhinids, in contrast, seem to represent an extremely early and rather specialized hypsilophodont divergence which failed to survive the close of the Triassic period.

There is a sporadic record of primitive-looking hypsilophodonts, apparently derived from the Triassic fabrosaurs, throughout the Jurassic and the Cretaceous. Hypsilophodonts are rare in the Lower Jurassic (Newman mentions[15] an unnamed example from the English Lias) and unknown in the Middle Jurassic. The Upper Jurassic record is very much better; hypsilophodonts occur in the Morrison formation of North America (*Laosaurus, Nanosaurus*) and in the English Purbeck (*Echinodon*). Furthermore, Kühne has discovered hypsilophodont teeth, rather like those of *Echinodon*, in the Kimmeridgian of Portugal[16]. Apart from *Laosaurus* (which may just cross the Jurassic/Cretaceous boundary) only three hypsilophodonts have been found in the Cretaceous—one (*Hypsilophodon*) in the English Wealden and two (*Thescelosaurus, Parksosaurus*) in the Upper Cretaceous of North America. This succession of hypsilophodont dinosaurs, extending from the Upper Trias through the Cretaceous, might best be envisaged as an evolutionary plexus in which each genus represents an individual strand. This concept of a plexus (rather than a simple lineage) lacks the implication that any one genus might be directly related to another. This hypsilophodont plexus is fundamental to the whole of ornithischian phylogeny; it represents the ancestry, ultimately at least, of such groups as the iguanodonts, hadrosaurs and ceratopsians.

Ornithischian Phylogeny

It now remains to examine the relationships between the hypsilophodonts and other ornithischians. One of the earliest known ornithischians (apart from the Triassic forms) is *Scelidosaurus*, an armoured and quadrupedal dinosaur from the Lower Lias of Dorset. This genus has often been regarded as a stegosaur, but Romer has demonstrated[11] that it is, in fact, an extremely early ankylosaur. *Scelidosaurus* resembles other ankylosaurs (or "armoured dinosaurs") in lacking any salient prepubis. So it is natural to conclude that the prepubis remained undeveloped throughout ankylosaur history. This conclusion dismisses the general assumption[14] that the ankylosaur pelvis had been derived from the typically ornithischian type of pelvis by reduction of the prepubis. *Scelidosaurus* probably shared a common ancestry with the hypsilophodonts of the Trias and so it becomes clear that the ankylosaurs, once thought to be an exclusively Cretaceous group, have an immensely long history. There are no records of ankylosaurs from Middle and Upper Jurassic rocks. The Cretaceous ankylosaurs have not yet been studied in detail and it is, at present, impossible to discern any distinct evolutionary lines within the group. The ankylosaurs are often considered to have been terrestrial reptiles but some, such as *Edmontonia*, possess a solid secondary palate, a feature which is almost certainly indicative of amphibious habits.

Another group of ornithischians, the family Iguanodontidae, first appears in the Middle Jurassic and persists until the Upper Cretaceous. The iguanodonts are clearly derivatives of the hypsilophodonts; they differ from the hypsilophodonts in being larger and more complex in structure. But there is some evidence that the family Iguanodontidae did not have a single origin among the hypsilophodonts (that is to say, that several groups of ornithischians have, at various times, crossed the hypsilophodont/iguanodont boundary). In support of this hypothesis, there are several ornithischian dinosaurs which exhibit a peculiar mixture of hypsilophodont and iguanodont characters; for example, *Dysalotosaurus*, from the Upper Jurassic of East Africa[17], which has sometimes been classified as a hypsilophodont, sometimes as an iguanodont. Since *Dysalotosaurus* has lost the more obvious hypsilophodont characters (the premaxilla is toothless and separates the maxilla from the nasal), it might best be regarded as an ornithischian which has just barely attained iguanodont status. A second example is furnished by the Upper Cretaceous *Thescelosaurus*[18]. This genus is invariably referred to the Hypsilophodontidae because it possesses premaxillary teeth and is very similar, in many respects, to the undoubted hypsilophodont *Parksosaurus*. But the hind limb of *Thescelosaurus* is typically iguanodont in appearance (that is, the femur is longer than the tibia). *Thescelosaurus* might therefore be considered as a hypsilophodont which shows a definite tendency towards the iguanodont grade of organization. The evidence from *Dysalotosaurus* and *Thescelosaurus* suggests that the family Iguanodontidae is a slightly artificial grouping and that it arose from the hypsilophodonts through iterative phases of evolution.

The origin of another ornithischian group, the suborder Stegosauria, presents even more of a problem. The armoured and quadrupedal stegosaurs (or "plated dinosaurs") appear in the Middle Jurassic and persist into the Lower Cretaceous. No Triassic or early Jurassic ornithischians are even vaguely suggestive of stegosaur ancestry. But the skull of *Stegosaurus* displays certain primitive characters; there is considerable contact between nasal and maxillary bones (in front of the orbit) and there is a broad and flat surface between the upper temporal fenestrae. Similar cranial features are evident in the Triassic hypsilophodont *Fabrosaurus* and in pseudosuchians such as *Euparkeria*. In most ornithischian dinosaurs there is no such nasal/maxilla contact and only a narrow zone separates the upper temporal openings. This evidence suggests that the stegosaurs were derived from the hypsilophodonts or (alternatively) that these two groups shared a common pre-Jurassic ancestry. It is unlikely that the stegosaurs could be related to either the ankylosaurs or the iguanodonts.

The origin of the suborder Ceratopsia (the "horned dinosaurs"), in contrast, is relatively easy to perceive. The Lower Cretaceous psittacosaurs (family Psittacosauridae) are clearly hypsilophodont derivatives which are highly suggestive of ceratopsian ancestry. These psittacosaurs resemble the hypsilophodonts in postcranial structure but show a slight advance towards the ceratopsian type of skull. Romer suggests[19] that *Psittacosaurus* possessed a beak-like rostral bone, diagnostic of ceratopsians, in front of the premaxillae. This trend towards ceratopsian structure is carried even further in the Upper Cretaceous family Protoceratopsidae.

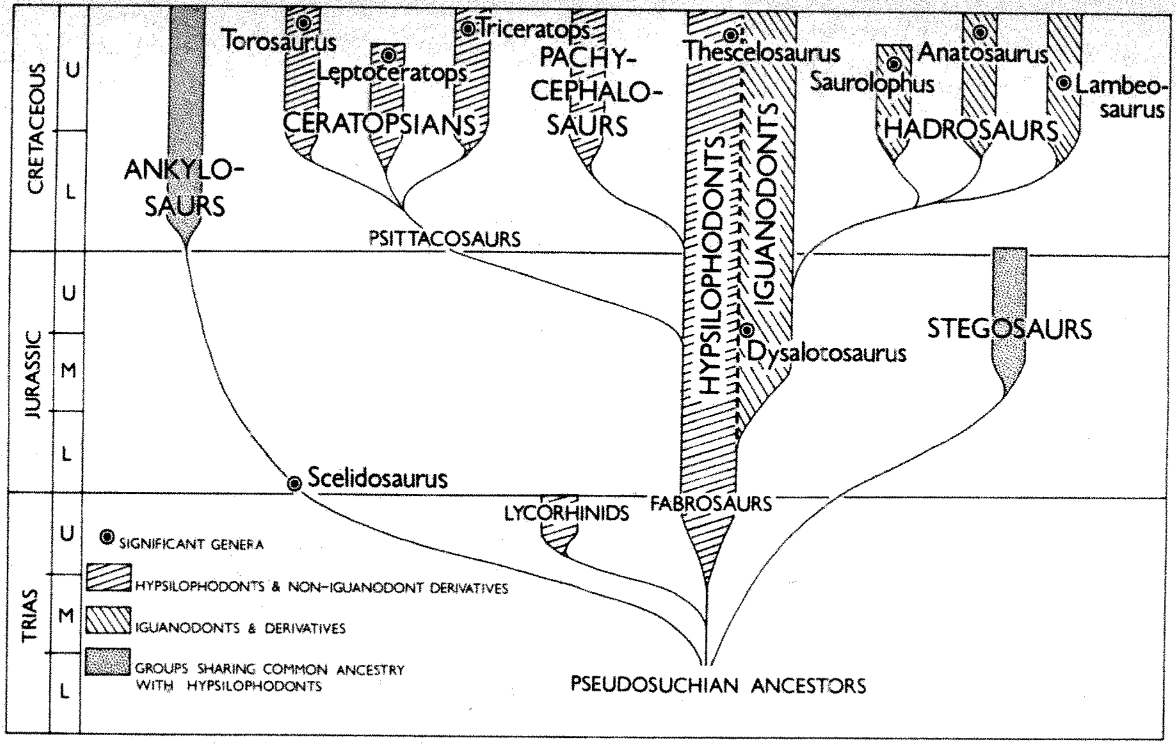

Fig. 4 Suggested phylogeny for the ornithischian dinosaurs.

The protoceratopsians are almost fully ceratopsian in appearance, but they still retain a few hypsilophodont characters; *Protoceratops*, for example, has teeth in the premaxilla. Even the true ceratopsians of the Upper Cretaceous—members of the family Ceratopsidae—display persistent traces of their hypsilophodont ancestry; *Triceratops*, perhaps the best known genus, has a primitive nasal/maxilla contact on the side of the snout. There can be little doubt therefore that the ceratopsians arose from the hypsilophodonts by way of psittacosaur and protoceratopsian stages. In a recent study of ceratopsian evolution Ostrom has discerned[20] three major lineages. One rather conservative lineage, terminating in *Leptoceratops*, seems to have retained the type of skull structure seen in *Protoceratops*. The members of a second lineage, exemplified by *Triceratops*, have the rear part of the skull extended into a moderately long bony "frill". The third ceratopsian trend, culminating in *Torosaurus*, involves extreme elongation of this cranial frill. Expansion of the frill is probably to be correlated with enlargement of the jaw muscles and with the development of a very powerful jaw action.

The Upper Cretaceous pachycephalosaurs (troödonts or "dome-headed dinosaurs") are characterized by a massively thick and solid roof to the skull. Apart from this peculiarity they conform to the hypsilophodont pattern of structure and they may be regarded, quite simply, as a late Cretaceous divergence from the hypsilophodonts. Galton suggests[21] that pachycephalosaurs used their armoured skulls as battering rams during competitive courtship display—rather like living goats and sheep.

Ostrom has concluded[22] that the Upper Cretaceous hadrosaurs (or "duck-billed dinosaurs") were derived from the iguanodonts by way of intermediates like the poorly known *Claosaurus*. Within the family Hadrosauridae, Ostrom recognizes at least three major lineages. The members of one lineage (for example, *Anatosaurus*) show relatively little advance on the cranial structure of their iguanodont ancestors. The other two lineages display the progressive development of hollow cranial "crests". One lineage includes hadrosaurs where the cranial crest is formed by extension of the nasals and the premaxillae (for example, *Lambeosaurus*). The other lineage comprises hadrosaurs, such as *Saurolophus*, where the crest is formed exclusively of the nasal bones. Furthermore, Ostrom has dispelled the popular concept of the hadrosaurs as aquatic or amphibious reptiles and has suggested[23] that these dinosaurs were active terrestrial foragers. More recently Galton has attempted to demonstrate some cursorial adaptations among the hadrosaurs[24].

All of the preceding discussion may be condensed into a single diagram (Fig. 4). This pictorial analysis of ornithischian phylogeny will doubtless require modification as new evidence comes to light but it would seem, for the present, to be a convenient summary of significant information. Such a scheme does at least emphasize the fundamental role of the hypsilophodonts in ornithischian history.

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Worldwide Deposition of Long-lived Fission Products from Nuclear Explosions

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The worldwide deposition of long-lived fission products is considered against the history of nuclear explosions. The present rate of deposition is much smaller than at the time of maximum fallout. The total amount deposited is consistent with the estimated amounts injected into the atmosphere.

THE radioactive debris from a nuclear weapon consists of fission products, unexpended fissile material such as uranium-235 and plutonium-239, and activation products—the result of the capture of excess neutrons in the weapon material or in the environment of the explosion. This vaporized mixture is forced upwards into the atmosphere by the tremendous release of energy in the explosion. As the cloud rises and cools, the radioactive products condense to form particles of solid debris. It is this particulate material, together perhaps with gaseous tritium (from fusion reactions) and carbon-14 (from the neutron reaction with atmospheric nitrogen), that later constitutes fallout. Nuclear radiations are emitted as the radioactive atoms disintegrate. The lifetime of the many products varies from fractions of a second to many years so that the radioactivity of the mixture decays in a complex manner.

Fission products from nuclear explosions have been present in the atmosphere for more than twenty years. At first the explosions were comparatively small so that the nuclear debris was confined zonally, within the troposphere and roughly to the latitude of the explosion sites. The stratosphere was penetrated for the first time by a thermonuclear device exploded by the United States in 1952. Since then there have been many large explosions[1] so that the subsequent dispersal of the debris, controlled by the meteorology of the stratosphere, has been world wide.

Of the fission products, caesium-137 (half-life thirty years) and strontium-90 (twenty-eight years) have, in the long term, the greatest biological significance in potential hazard to human populations. Since 1954 the concentration of these fission products has been observed at Harwell in rain from a number of collecting stations. Samples of rainwater are collected for periods of three months at (currently) twenty-eight stations[2] between latitudes 70° N and 76° S, including eight stations in the United Kingdom. The details of the techniques of sampling and analysis have been described by Cambray *et al.*[3].

The worldwide deposition of long-lived fission products may be calculated by the method of Stewart *et al.*[4] by integrating the distribution by latitude of the concentration in rain, weighted by the distribution by latitude of rainfall[5]. Because all the sampling stations are based on land it is necessary to assume that the concentrations measured in rain and the amount of rainfall are representative also of the oceans in the same latitude zone. The record for strontium-90 obtained by this means by Cambray *et al.*[2] is given in Fig. 1. This shows the annual deposition in northern and southern hemispheres, the total deposition and the calendar of high yield nuclear explosions[2,6-8]. The low yield of tropospheric explosions have been ignored. Conventionally, the uncertainty attributed to the plotted points is 20% or 0.1 megacuries (MCi), whichever is the larger.

Annual Deposition

The shapes of the deposition curves conform generally to the calendar of nuclear explosions. Thus the annual rate of deposition increased to a maximum in 1959, the year following the first phase, during which about 90 "megatons of fission yield" were produced[1]. There was a rapid decrease in 1960, a quiescent year, before explosions started again late in 1961. This massive series, yielding another 100 Mton, ended in 1962, and was followed by a peak in deposition rate during 1963 and then a steady fall until 1967. In this year the third phase of nuclear weapon testing started, a period of occasional explosions. (100 Mton of fission yield ~10 MCi of strontium-90 and corresponding quantities of other fission products.)

In the first phase of (high yield) nuclear explosions, before 1959, the individual explosions were usually of moderate size and took place at or near ground level. Much of the debris, including surface material entrained in the updraught, would have been lodged in the lower stratosphere. From here descent into the troposphere was prompt and in accordance with the subsidence mechanism that occurs (in the northern

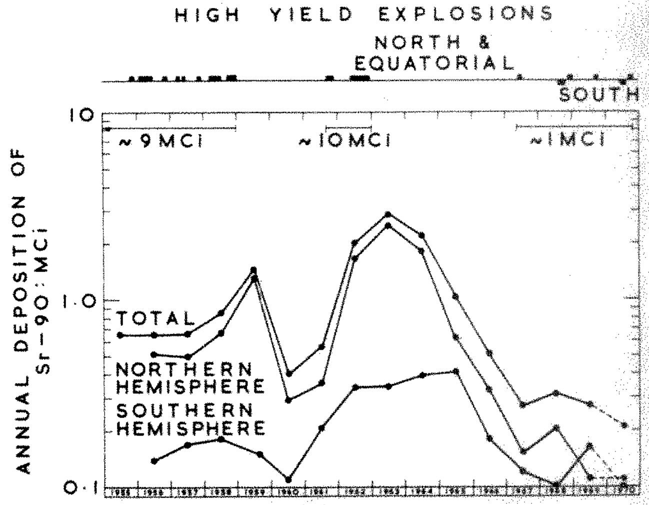

Fig. 1 Annual deposition of strontium-90.

hemisphere) in the early months of each year[9]. This explains the sharp decrease in deposition rate between 1959 and 1960. On the other hand, during the second phase 1961–62 the individual explosions were larger and generally above ground level. This implied insertion of debris higher in the atmosphere. The subsequent decrease in the total deposition rate—during the period 1964–67—was regular and more gradual, suggesting that the residence of the debris was controlled by a more general atmospheric mechanism, and not only by the sharp seasonal subsidence from the lower stratosphere. The characteristic rate of decrease was equivalent to a mean residence time in the stratosphere of sixteen months, or a half-residence time of eleven months. This estimate of residence time agrees with that obtained directly by Feely *et al.*[10] from observations of the strontium-90 content of the stratosphere, sampled from aircraft and balloon.

During the period of regular reduction in the total annual deposition, the rate of deposition in the southern hemisphere increased in spite of the absence of high yield explosions during 1963–66. This has been explained[11,12] by an exchange of debris between hemispheres, equivalent to a mean residence time against inter-hemispheric transfer of three to five years. The increase in the south was balanced by a decrease in the north at a rate faster than in the total deposition (Fig. 1). Therefore the residence time as observed at a northern station during this period would seem somewhat shorter than the real residence time against fallout.

The steady fall in total deposition rate continued until by 1967 the level was about one-tenth of the maximum in 1963. In 1967 the third phase of nuclear weapon testing started, yielding a few megatons during each of the years 1967–70. Because the total annual deposition has been approximately constant during this current phase the rate of injection of strontium-90 into the stratosphere was seen to be in fortuitous balance with the rate of depletion of the reservoir. This balance is also indicated by the high proportion, in debris observed at ground level during 1969 (ref. 8) and 1970 (ref. 2), from recent Chinese and French explosions.

The excess of strontium-90 deposited in the northern hemisphere over that in the southern hemisphere reflects the asymmetric injection of debris. The injections from the Russian sites at 52° N and 75° N have been largely contained within the hemisphere: the equatorial injections have been shared according to the latitude and season of the event[9].

Throughout the whole period of observation the concentrations of long-lived fission products in surface air and rain, measured at a particular station, are related to the worldwide deposition. Thus comparison of strontium-90 deposited annually (MCi) in the northern hemisphere with the annual mean concentration (pCi/kg) in surface air at Chilton[2] (51½° N, 01° W) gives a ratio that lies, within a factor of two, about 10^{20} kg. This ratio incorporates the latitude factor appropriate to Chilton and smoothes out the seasonal variation[4,9,13].

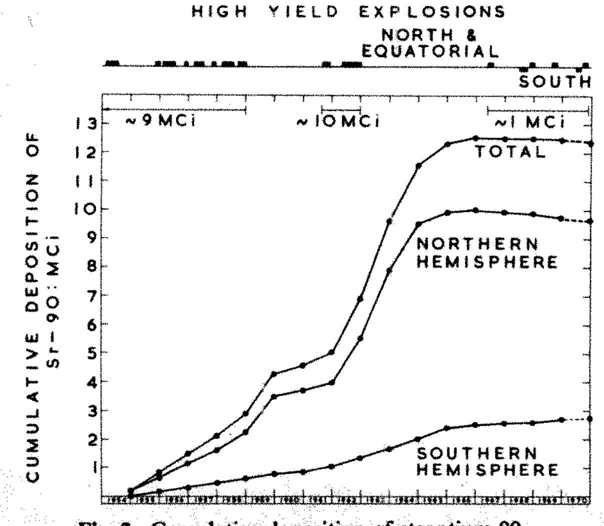

Fig. 2 Cumulative deposition of strontium-90.

Cumulative Deposition

An alternative description of the history of the deposition of strontium-90 is given in Fig. 2, which shows the cumulative amounts corrected for radioactive decay. Although the annual deposition in the southern hemisphere has recently approached that in the northern hemisphere, the accumulated deposit in the north remains about four times that in the south. The pause between the first and second phases of nuclear testing is shown by the plateau in 1960–61 at about 4.5 MCi (total). This does not account for the whole of the strontium-90 produced up to that time: apart from radioactive decay and the residue in the stratospheric reservoir, some 3 MCi was deposited in the vicinity of the explosion sites[1]. The second plateau, since 1966, represents an approximate balance between rate of deposition and radioactive decay of the strontium-90 already deposited.

The results obtained from these sampling stations[2] may be compared with the results from those operated by the United States Atomic Energy Commission[14]. The ratios of the worldwide deposition, estimated annually over the period 1958–69, have a mean (Harwell/USAEC) of 0.99 ± 0.10 s.d. The cumulative deposit of strontium-90 at the end of 1969 estimated in the present work is 12.42 MCi, compared with the American estimate[14] of 12.25 MCi. In addition, the Harwell estimate of the cumulative deposit at the end of 1967 is 12.5 MCi: this compares with the value of 13 MCi derived by Hardy *et al.*[15] from analyses of soil samples.

Because the extrapolation required from small samples to the global scale is so great that systematic errors might be expected to outweigh the random uncertainties, the agreement is surprisingly good. Each laboratory, using a separate sampling system and different methods of analysis and global integration, has achieved the same result, within experimental error. This result accords with the estimates[1] of injection, after making allowance for "close-in" fallout and for radioactive decay. Although it would be unreasonable to claim absolute accuracy, it is thus possible to account for the worldwide deposition of the long-lived fission products in a manner that is consistent, quantitatively, with the amounts that have been produced in nuclear explosions.

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Light Chains from Fast and Slow Muscle Myosins

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Myosin from fast skeletal muscles consists of two large subunits (each about 200,000 daltons) and approximately four smaller subunits (in the range of 20,000 daltons). The light chains are heterogeneous in both size and charge, irrespective of the muscle type of origin. Moreover, the myosins from fast muscles of several species show a characteristic light chain pattern which is distinct from that of slower muscles.

THE bulk of the myosin molecule is composed of two large polypeptide chains each with a mass of about 200,000 g/mol[1-3], but some 10 to 15% of myosin seems to consist of low molecular weight material[4-7]. These "light chains" are thought to be involved in regulating the hydrolytic activity of myosin[8,9]. A persistent problem associated with studies on the light chains has been the origin of their electrophoretic heterogeneity. The possibility exists that some of this heterogeneity may in fact arise from tightly bound contaminants or chemical modification of the proteins during their isolation. We shall describe a procedure whereby myosin from different species and types of muscle may be purified rapidly and the light chains compared in mass and charge.

By blocking the sulphydryl residues of the light chains, it is possible to obtain a simple electrophoretic gel pattern with two to three bands whose relative proportions remain approximately the same with or without the presence of sodium dodecyl sulphate (SDS). Mobility in SDS gels permits an accurate determination of the mass of the components[10-12] while mobility in standard gels reflects the charge profile, so that the two electrophoretic techniques combined provide a sensitive "fingerprint" for comparing light chains from a variety of muscle tissues. Moreover, microdensitometer traces of 5 and 10% SDS gels can be used to estimate the number of moles of light chains in the myosin molecule.

Subunit Composition of Myosin

Polyacrylamide gel electrophoresis of rabbit skeletal (white) myosin in the presence of SDS shows predominantly three low molecular weight bands[11]. Comparison of the electrophoretic mobilities with those of proteins of known molecular weight gives values of 25,000, 18,000 and 16,000 ± 5% for the three fastest migrating species (Fig. 1*a*). Lying between these components and the heavy chains (at the top of the gel) are minor bands in the 150,000 molecular weight range. This material can be almost entirely removed by ion exchange chromatography of myosin on DEAE-cellulose and probably represents a contaminant of myosin (Figs. 1*c* and 2). The remaining electrophoretic bands are unaffected by all current purification procedures: exposure to 4.7 M NH_4Cl[13] does not result in any selective removal of light chains (Fig. 1*b*), nor does fractionation with saturated $(NH_4)_2SO_4$ in the presence of 2.5 M LiCl affect the pattern (Fig. 4*a* and *b*)[14]. Light chains can, of course, be removed by treatment of myosin with alkali or guanidine hydrochloride or high concentrations of lithium salts, but these procedures inevitably lead to complete loss of ATPase activity. The only procedure described so far which

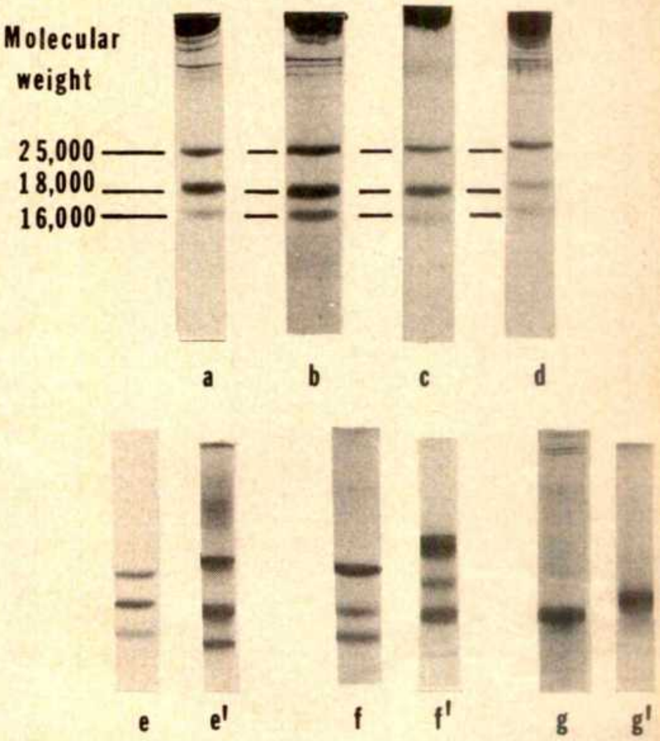

Fig. 1 Polyacrylamide gel electrophoresis of rabbit skeletal myosin and its light chains. (*e′*, *f′*, *g′*) are standard 7% acrylamide gels (*p*H 8.5) prepared according to the Canalco manual. All others are 10% SDS acrylamide gels prepared according to Weber and Osborn[11]. Myosin was routinely dialysed against 8 M urea, 0.01 M sodium phosphate, *p*H 7, containing 0.1% SDS and 0.1% β-mercaptoethanol. Molecular weights were determined from standard curves[11] and by running proteins of known molecular weight (chymotrypsinogen, β-lactoglobulin and myoglobin) together with the myosin. All isolated light chains shown here (*e*–*g*) were modified by performic acid oxidation (PAO) (for details, see ref. 17). *a*, Myosin prepared by conventional reprecipitation at low ionic strength. *b*, Myosin exposed to 4.7 M NH_4Cl for 10 min and precipitated with saturated $(NH_4)_2SO_4$ containing 4.7 M NH_4Cl, according to Gershman and Dreizen[13]. *c*, Myosin purified by DEAE-cellulose chromatography[25]; see Fig. 2 for details. *d*, Myosin treated with 0.01 M DTNB, 0.05 M Tris, *p*H 8.5, 0.5 M KCl, 1 M urea (sometimes omitted) for 15 min[3,15,17] and precipitated by ten-fold dilution. *e*,*e′*, Total light chains from myosin. *f*,*f′*, Light chains from DTNB-treated myosin (see *d*). *g*,*g′*, Light chains from supernatant of DTNB reaction.

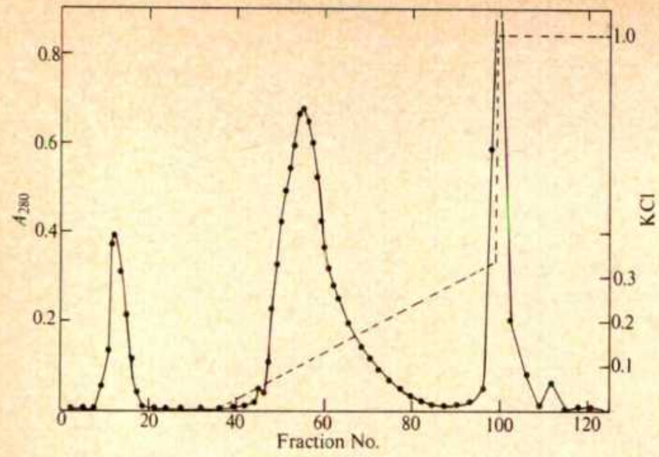

Fig. 2 Chromatographic purification of myosin. Minced muscle (in this case the anterior latissimus dorsi from chicken, 11 g) was extracted with 0.3 M KCl, 0.15 M phosphate, *p*H 6.5, 0.02 M EDTA, 5 mM $MgCl_2$, 3.3 mM ATP for about 30 min with stirring in the Sorvall blender. The extract was precipitated by a ten-fold dilution and taken up in 0.04 M $Na_4P_2O_7$, *p*H 7.5, against which it was dialysed. About 100 mg protein in 20 ml. was applied to a 30×1.5 cm DEAE (Whatman DE-52) column equilibrated with 0.02 M $Na_4P_2O_7$, *p*H 7.5. The protein was eluted with a linear gradient (0 to 0.5 M KCl in 0.02 M $Na_4P_2O_7$) of 400 ml. Fractions 47–71 were combined, dialysed exhaustively against 1% acetic acid and freeze-dried; the yield was 57 mg.

removes an appreciable portion of a light chain fraction without significantly altering the enzymatic activity is the reaction of myosin with 5,5′-dithiobis-(2 nitrobenzoic acid) (DTNB)[3,15]. The light chains released by DTNB consist essentially of the 18,000 molecular weight species (Fig. 1*d*, *f* and *g*). (The same patterns could be obtained with myosin from chicken breast muscle.) After unblocking the DTNB-treated myosin with dithiothreitol, the Ca-ATPase, the EDTA-activated ATPase, and the actin-activated Mg-ATPase are about 70–80% of the control myosin. We were unable to find conditions in which all the light chains of 18,000 molecular weight dissociate. It required denaturation by alkali or guanidine hydrochloride to remove the remaining 18,000 molecular weight subunits as well as the 25,000 and 16,000 molecular weight components (Fig. 1*e* and *f*).

Most of the literature on light chains characterizes these subunits by some form of electrophoresis such as cellulose acetate strips[9] or disc gel electrophoresis[16] in standard buffers. The number of bands thus displayed has been variable and no clear picture of the composition of the light chains has emerged. The inclusion of SDS in the buffer system greatly simplifies the electrophoretic pattern; however, this procedure limits the characterization to one of size rather than charge. An equally simple pattern can be obtained in the absence of SDS if all the sulphydryl residues of myosin are chemically blocked—preferably by performic acid oxidation[17]. The isolated light chains from the oxidized myosin show the same number of bands and approximately the same distribution of stain on the standard *p*H gels (Fig. 1*e′*–*f′*) as on the SDS gels (Fig. 1*e*–*f*). Thus there are predominantly three kinds of light chains in rabbit skeletal myosin—by the criterion of mass and charge. The 16,000 and 25,000 molecular weight subunits seem to be chemically related in sequence[17–19], whereas the 18,000 molecular weight subunit, or DTNB-light chain, is chemically quite distinct[15,17] (see following article[20]). As shown later, this light chain pattern will vary somewhat depending on the type of muscle from which the myosin is derived.

Stoichiometry of Subunits

Physical chemical methods for determining the moles of light chains in myosin cannot be used to discriminate among the three different classes of light chains in rabbit skeletal (white) myosin. Values derived from light scattering[21], sedimentation velocity and sedimentation equilibrium measurements have ranged from 2 to 3 mol of total light chains per mole myosin[2,13]. The application of the "radioisotope dilution" technique to the problem of the stoichiometry showed that myosin contained 2 mol of DTNB-light chains and 2 mol of alkali-dissociated light chains[17]. Although chemical methods have the drawback of requiring large amounts of highly purified individual light chains, they are undoubtedly the most reliable means for determining stoichiometry. For obtaining a first approximation of the moles of light chains on small samples of whole myosin, however, a quick and relatively simple procedure is to measure the relative concentrations of protein in the light and heavy chain bands on SDS polyacrylamide gels. Such an approach is hardly new; one of the best examples of its application has been the determination of the stoichiometry of the twenty or so proteins in the ribosome[22].

Owing to the great disparity in size and amount of light chains relative to heavy chains, it was considered best to run the myosin simultaneously on both 5 and 10% acrylamide gels. A known volume of a stock myosin solution was layered on each gel, with a minimum of ten times the concentration of myosin on the 10% as on the 5% gels. Since one must ultimately relate the concentration of myosin on the 5% gels to that on the 10% gels, the accuracy of the final calculation of light chains will depend in part on how precisely all volumetric

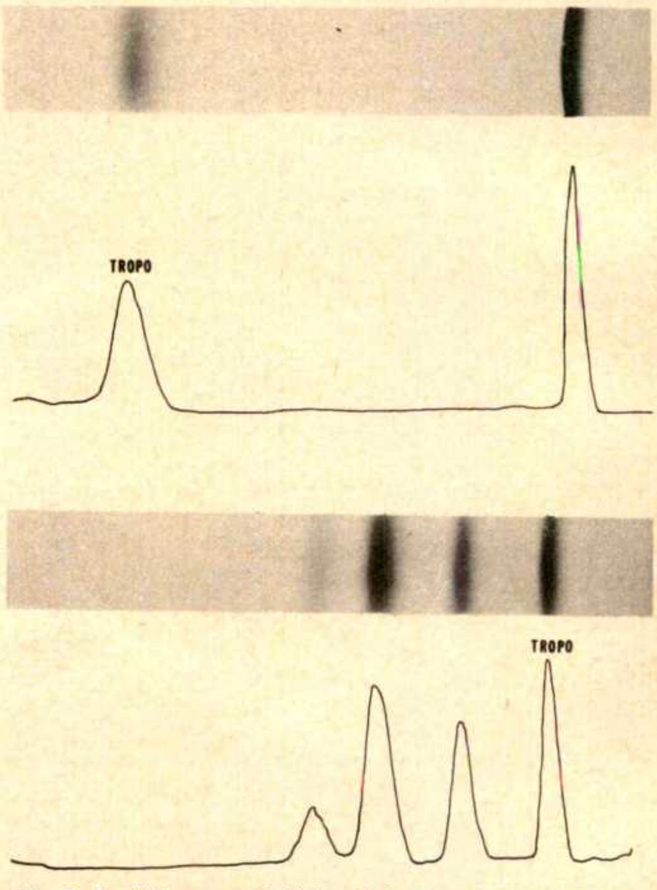

Fig. 3 Stoichiometry of light chains by densitometry of SDS gels. Samples of proteins were applied directly to the top of the gel with a 0.1 ml. Hamilton syringe. Gels were run about 5 h at 8 mA per tube, fixed overnight in 45% methanol, 9.2% acetic acid[11], and stained for 1 h in the same solvent containing 0.25% Coomassie brilliant blue or 0.5% aniline blue–black. Gels were destained electrophoretically and scanned on a Joyce-Loebl recording microdensitometer. The areas of the peaks (magnified about ×5) were measured by planimetry and recorded as an average of 5 readings. Top, 5% SDS gel loaded with 100 µl. of 0.1 mg/ml. tropomyosin and 100 µl. of 0.1 mg/ml. myosin. Bottom, 10% SDS gel loaded with 100 µl. of 0.1 mg/ml. tropomyosin and 150 µl. of 2.4 mg/ml. myosin.

dilutions and applications of sample are made. Another potential source of difficulty is the different degree of staining of the 5 and 10% gels. To minimize this error, an equal amount of tropomyosin (molecular weight, 64,000) was applied to both gels, and any difference in area between the densitometer traces of the 5 and 10% gels was used to correct for differences in uptake of stain. A typical experiment is shown in Fig. 3. The heavy chains are unable to penetrate the 10% gels, but migrate well on the 5% gels. The light chains are well resolved on 10% gels but diffuse too much on 5% (or even 7%) gels to permit optimal microdensitometer traces. In using microdensitometry to determine protein concentration, it is imperative to demonstrate that the optical densities being measured are well within the linear range of the instrument. This was shown by running eight gels with increasing loads for each experiment. Plots of densitometer area versus load (or concentration) were reasonably linear and obeyed Beer's law. Results from several such determinations are summarized in Table 1. A striking feature of these data is the relatively constant value of total light chains for all these different myosins, despite variations in number and amounts of different light chains.

The validity of this approach depends largely on the extent to which the uptake of dye is affected by variations in the amino-acid composition of the subunits. Ideally, the degree of staining should depend only on protein concentration and be independent of the primary structure of the protein. Although the ideal situation is undoubtedly not realized, there are several reasons for believing the staining error to be small. (1) Our conclusions regarding the stoichiometry are in essential agreement with the chemical data on rabbit (white) myosin[17]. (2) The use of either Coomassie brilliant blue or aniline blue–black led to approximately the same results. (3) A study in which several dyes were used to estimate protein concentration reported a variation of about ±10% in absorbancy for a series of unrelated proteins of identical concentration[23]. (4) Preparations of isolated light and heavy chains from rabbit skeletal myosin, the concentrations of which had been determined by Kjeldahl nitrogen, were run on 10% and 5% gels respectively and stained with aniline blue–black. The microdensitometer traces of the stained heavy and light chains were found to be identical for an equivalent amount of applied protein.

The results in Table 1 suggest that myosin from fast skeletal muscles contains approximately 4 mol of light chains: 2 mol of an 18,000 dalton subunit and a total of 2 mol of the 25,000 and 16,000 dalton subunits. Myosins from slow muscles seem to have equimolar amounts of a 27,000 and 20,000 dalton subunit. In the absence of more detailed chemical data on the separated light chains from cardiac and anterior latissimus dorsi myosin, the stoichiometry must be regarded as tentative.

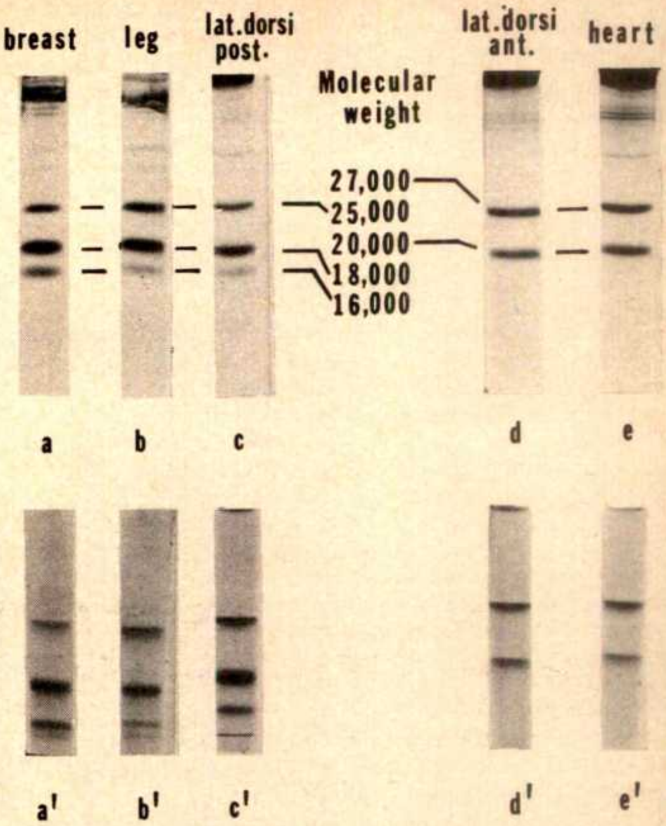

Fig. 4 Light chains from chicken muscles. All myosins were purified on the type column described in Fig. 2. Myosins from leg and breast muscles were in addition fractionated with $(NH_4)_2SO_4$ in the presence of 2.5 M LiCl[14]. *a* to *e* are 10% gels. *a'* to *e'* are PAO light chains prepared from the above myosins and run on 7% standard gels. Myosins were from: *a*, breast muscle; *b*, red leg muscles; *c*, the posterior latissimus dorsi muscle; *d*, the anterior latissimus dorsi muscle; *e*, cardiac muscle.

Comparative Studies

The light chains from various fast muscles show predominantly three classes of subunits either in SDS gels (Fig. 4*a*, *b* and *c* and Fig. 5*a* and *b*), or in standard acrylamide gels (Fig. 4*a'*, *b'* and *c'* and Fig. 5*a'* and *b'*). The pattern seems to be independent of species (in addition to chicken and rabbit myosins, sheep skeletal myosin shows the same three bands on SDS gels), and depends only on muscle type. The slower muscles, such as the anterior latissimus dorsi muscle or cardiac muscle, show two classes of light chains in the presence or absence of SDS (Fig. 4*d* and *e* and Fig. 5*c*). In addition to missing a 16,000 molecular weight subunit, the slow muscle

Table 1 Stoichiometry of Light Chains

Light chain	Rabbit leg and back		Rabbit white		Chicken breast		Chicken ant. l. dorsi		Chicken heart	
	%	(mol)	%	(mol)	%	(mol)	%	(mol)	%	(mol)
16,000	17	(0.8)	16	(0.7)	26	(1.2)	—	—	—	—
18,000	51	(2.2)	55	(2.0)	47	(1.9)	—	—	—	—
20,000	—	—	—	—	—	—	45	(2.0)	45	(1.6)
25,000	32	(1.0)	29	(0.8)	27	(0.8)	—	—	—	—
27,000	—	—	—	—	—	—	55	(1.8)	55	(1.5)
% total light chains in myosin	16.8±1		14.1±1		15.8±2		19.3±2		14.7±1	

The value for the % of each light chain relative to the total light chain content (as measured in densitometer areas) represents an average of six to eight gels stained with both CBB and ABB. For "the percentage of total light chains in myosin" the contribution of the heavy chain needs to be determined; in this case, only ABB gels were measured, this dye giving more reproducible results than CBB. To determine the moles of light chain, a value of 470,000 daltons was assumed for all myosins. For example: moles of DTNB-light chain in rabbit white myosin = (14.1%) (55%) (470,000)/(18,000) = 2.0.

myosins have light chains of slightly higher molecular weight than those in fast muscle myosin. The absolute values of the molecular weights are not as significant as the fact that mixtures of slow and fast muscle myosins show band splitting in the 25,000 and 20,000 region, with the slow muscle light chains higher in molecular weight than those of the fast muscles. Thus the heterogeneity of the light chains observed in fast muscle myosin cannot be explained on the basis of contamination by slow muscles, as has been previously proposed.

Red muscle myosin from rabbit interestingly shows a split band in both the 25,000 and the 20,000 region of the SDS gel pattern and a faint band in the 16,000 position (Fig. 5*d*). The standard gels are, paradoxically, too sensitive to minor changes in structure to show this band splitting. Major bands, in the standard gels, are generally bordered by several minor bands due to slight chemical modification of the side chains or aggregation or both. The SDS gels which are only sensitive to mass, however, suggest that the bands for the red muscle myosin represent a mixture of white myosin light chains and a pair of light chains similar in mass to those of cardiac or anterior latissimus dorsi myosins. To prove this point, two separate mixtures were run: one had white muscle myosin added to red muscle myosin, and the other had cardiac myosin added to red muscle myosin (Fig. 6). It is clear by inspection of the gels and their densitometer traces that the white myosin enhanced the 25,000, 18,000 and 16,000 molecular weight positions while the cardiac myosin enhanced the higher molecular weight bands in the 27,000 and 20,000 range. Thus it seems as if a so called pure red muscle may exist which has essentially two kinds of light chains.

This simple picture of a relationship between the light chain pattern and the speed of the muscle may, of course, be an over-simplification, based as it is on a limited study. However, for the present, it is tenable to hypothesize that the light chains may contribute to determining the response of the muscle by regulating the active sites of myosin[8,9,24].

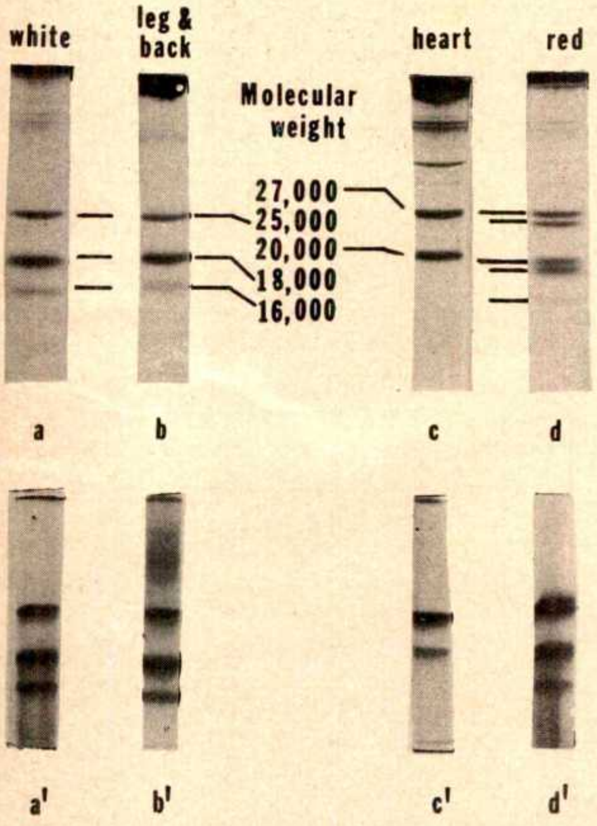

Fig. 5 Light chains from rabbit muscles. All myosins are column purified (see Fig. 2). *a* to *c* are 10% SDS gels; *d* is a 12.5% SDS gel. *a'* to *d'* are PAO light chains from the above myosins and run on 7% standard gels. Myosins were from: *a*, the white vastus lateralis muscle; *b*, the leg and back muscles; *c*, cardiac muscle—the additional strong band is actin; *d*, red muscles, including semitendinosus and crureus.

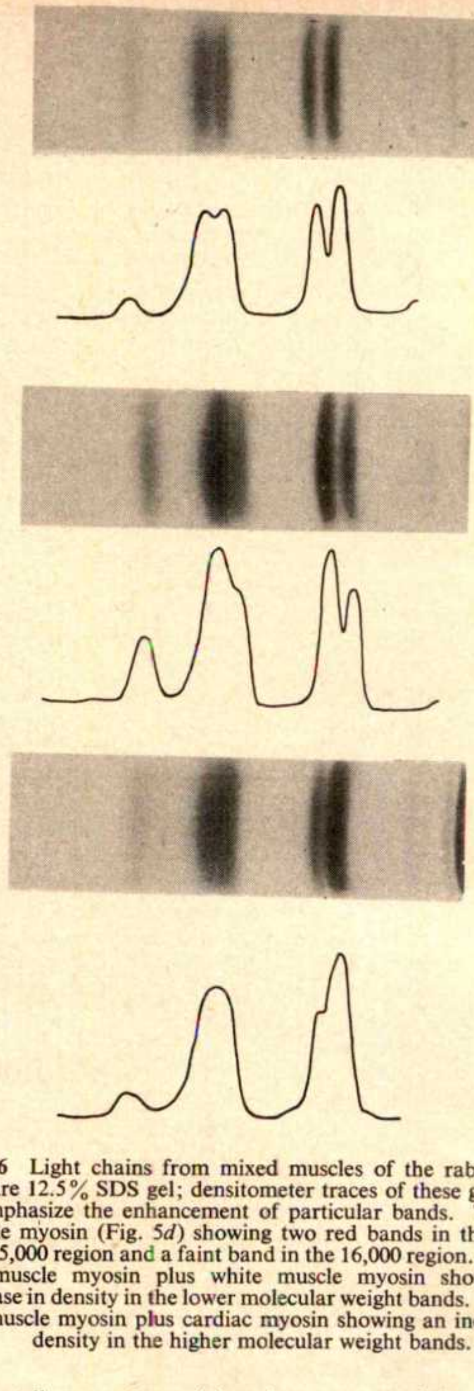

Fig. 6 Light chains from mixed muscles of the rabbit. All gels are 12.5% SDS gel; densitometer traces of these gels serve to emphasize the enhancement of particular bands. Top, red muscle myosin (Fig. 5*d*) showing two red bands in the 20,000 and 25,000 region and a faint band in the 16,000 region. Middle, red muscle myosin plus white muscle myosin showing an increase in density in the lower molecular weight bands. Bottom, red muscle myosin plus cardiac myosin showing an increase in density in the higher molecular weight bands.

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Chemical Studies on Light Chains from Cardiac and Skeletal Muscle Myosins

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Differences have been observed in the thiol sequences of light chains from cardiac and skeletal muscle myosins. Cardiac light chains from both bovine and sheep hearts contain the same thiol sequence (peptide A) which is present in the "alkali" light chains of rabbit and sheep skeletal myosin, but have two extra thiol sequences (peptides B and C). Chemical similarities have been demonstrated between myosin light chains from cardiac and slow skeletal muscle.

CHEMICAL studies of the light chains of rabbit skeletal muscle myosin have shown that these exist in two distinct classes as characterized by their thiol sequences[1,2], although electrophoresis on polyacrylamide gels and cellulose acetate indicates more extensive heterogeneity[3-5]. One of these light chains can be removed selectively from myosin by reaction with 5,5′-dithiobis-(2 nitrobenzoic acid) (DTNB)[2,6], in conditions where ATPase activity is little affected. This light chain gives a single band on polyacrylamide gels of molecular weight 18,000 and contains two thiol groups in identified sequences (peptides 1 and 2)[2]. This we term the DTNB-light chain. The other chemical class of light chain is characterized by a single thiol sequence (peptide A), but gel electrophoresis shows the presence of two components of different molecular weights[1]. These two light chains, together with any remaining DTNB-light chains, can be removed from myosin in various conditions, including alkaline *p*H[7], acylation[8], or treatment with denaturing agents such as urea or guanidine hydrochloride[6,9]. We shall refer to these light chains not dissociated by the DTNB reaction as the "alkali" light chains[1]. The stoichiometry of these two classes of light chains has been determined both by isotope dilution[1] and by densitometry of polyacrylamide gels[10], showing that there are 2 mol of the DTNB-light chains and 2 mol of the "alkali" light chains per mol of myosin, consistent with its bipartite structure[11]. Examination of the active papain fragment of myosin, HMM S-1, shows that there is 1 mol of the "alkali" light chain in each HMM S-1, but the DTNB-light chain seems to be partially degraded during papain cleavage[1]. If the light chains are dissociated from HMM S-1 or from myosin in mild conditions with 4 M lithium chloride, they can be reassociated with the heavy chains to recover enzymatic activity[12,13]. Thus they seem to be involved in the hydrolytic activity of myosin.

Light chains of myosins from various animals give different mobilities on gel electrophoresis[14], and SDS gels have confirmed differences in the molecular weights of light chains from fast skeletal muscle myosin and cardiac myosin (preceding article[10,25] and our unpublished observations.) It was therefore important to examine the thiol sequences of cardiac light chains to establish whether they were related to the light chains from skeletal muscle myosin. Because of the limited size of rabbit hearts, cardiac myosin was prepared from beef and sheep hearts, and to ensure that differences might not be species specific, a comparative study was carried out with sheep skeletal muscle myosin.

The myosin was prepared from sheep leg muscle by standard methods[1], and from cardiac myosin as described before[15]. Treatment with DTNB was carried out as described previously[1,6], while the remaining light chains were dissociated from myosin by incubation in 4 M urea for 2 h at room temperature in the presence of 5 mM EDTA and 2.5 mM dithiothreitol at *p*H 8.0, followed by ten-fold dilution with ice cold water to precipitate the heavy chains. The light chains were recovered from the supernatant by freeze drying or by concentrating with a DEAE-cellulose column[1]. Carboxymethylation with ^{14}C-iodoacetic acid was carried out as described before[1]. Gel electrophoresis was performed according to the Canalco-Chemical Formulation of Disc Electrophoresis (1965).

The carboxymethylated light chains were digested with α-chymotrypsin overnight at room temperature in 0.1 M ammonium acetate at *p*H 8.0 using an enzyme : substrate ratio of 1 : 80 (w/w) and a light chain concentration of 1–4 mg/ml. The digests were freeze dried, then dissolved in *p*H 6.5 pyridine acetate electrophoresis buffer diluted 1 : 1 with water, and applied to Whatman No. 3 MM paper at a loading of 1 mg/cm for electrophoresis at *p*H 6.5 (see ref. 20 for details of buffers). The radioactive peptides were further

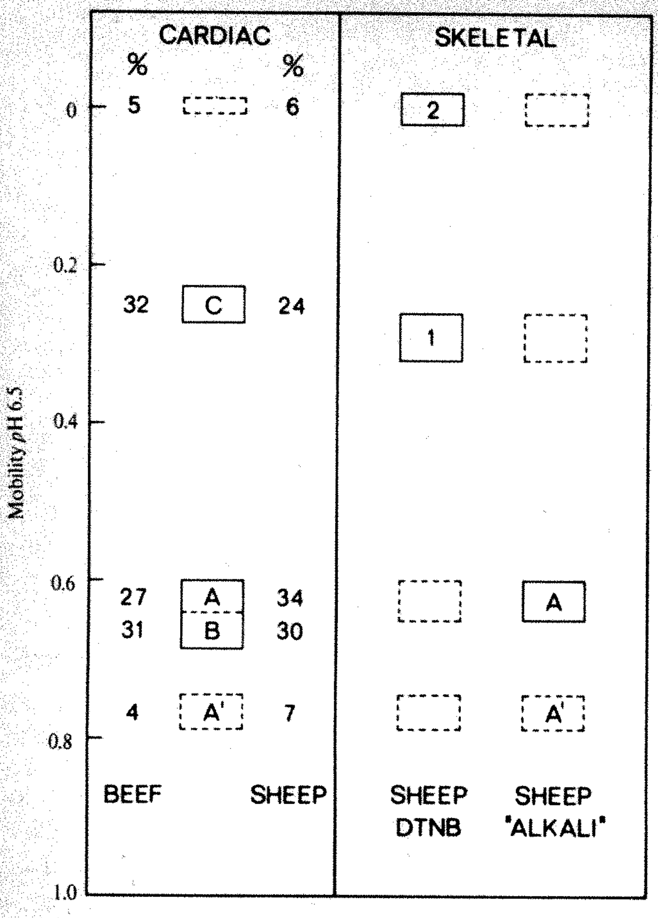

Fig. 1 Mobilities at pH 6.5 of radioactive CMCys peptides from chymotryptic digests of cardiac and skeletal myosin light chains expressed relative to aspartic acid = 1.0 (ref. 17). □, strong radioactive peptides; ⬚, weak radioactive peptides. The percentage counts in each peptide were calculated for a single preparation of sheep cardiac light chains, and two preparations of the beef light chains. The nomenclature of the peptides is given in the boxes. (The mobilities of the peptides from sheep skeletal muscle were identical to those from rabbit muscle[1].)

purified by electrophoresis at pH 2 and strips containing them were exposed to performic acid vapour to produce the sulphone derivative of the carboxymethylcysteine; final purification was achieved by electrophoresis at pH 3.5. The peptides were eluted from the paper with pH 6.5 electrophoresis buffer diluted 1:4 with water. Amino-acid sequences were determined by the dansyl-Edman method[16], and amide assignments made on the basis of pH 6.5 mobility changes after removal of aspartic or glutamic acid residues with the Edman reagent[17].

Beef Cardiac Light Chains

Beef cardiac myosin was treated successively with DTNB and 4 M urea as described. Both supernatant fractions were reacted with ^{14}C-iodoacetic acid and examined by gel electrophoresis. The light chains from the urea treatment gave two major bands, while those from the DTNB reaction showed the same two bands but in considerably reduced amounts. To confirm that these two fractions were similar, the proteins were digested with chymotrypsin and submitted to electrophoresis at pH 6.5. Autoradiographs showed the same three peptide bands for both the light chains dissociated by urea and those dissociated by DTNB. Thus the DTNB reaction removed a small amount of the total light chains, rather than a specific component as for rabbit skeletal muscle myosin. The amount of protein dissociated from cardiac myosin by DTNB was less than 1.5% of the myosin compared with 5–6% for rabbit skeletal myosin.

Thereafter, for larger scale preparations from beef cardiac myosin, the DTNB treatment was omitted and the total light chains were dissociated by urea incubation. Chymotryptic digests of the carboxymethylated derivatives were fractionated by electrophoresis at pH 6.5, giving three major and two minor radioactive peptide bands (Fig. 1). (Peptides A and B did not always separate, but with longer electrophoresis times two bands could be clearly discerned.) The percentage of counts in each band (Fig. 1) showed that the three major peptides occurred in roughly equal yield. The peptides were further purified by electrophoresis at pH 2, though the number of radioactive spots obtained at this pH was somewhat variable. The additional heterogeneity could be attributed to partial oxidation of the CMCys to CMCys sulphone which produces pairs of spots in the pH 2 dimension (Fig. 2). Such oxidation could be avoided by including thiodiglycol (0.5% v/v) in the wetting buffers, and this was necessary to facilitate separation of peptides A and B. Strips containing the radioactive peptides from the pH 2 electrophoresis were oxidized with performic acid vapour in a desiccator[18] and final purification achieved by further electrophoresis at pH 3.5.

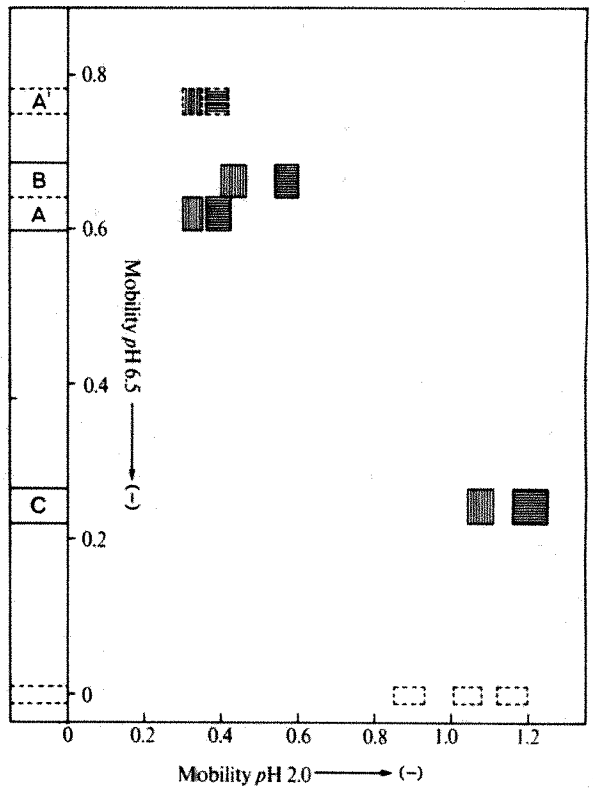

Fig. 2 Two dimensional peptide map of radioactive CMCys peptides from chymotryptic digests of beef cardiac myosin light chains. Mobilities at pH 6.5 expressed relative to aspartic acid = 1.0, and at pH 2 relative to serine = 1.0 (ref. 17). □, Strong radioactive peptides; ⬚, weak radioactive peptides; ▥, unoxidized CMCys derivatives; ▤, oxidized CMCys sulphone derivatives. The nomenclature of the peptides is given in the pH 6.5 dimension.

The mobilities of peptides A and A′ were the same in all electrophoretic conditions as peptide A and its deamidated derivative from rabbit "alkali" light chains[1,2], and the amino-acid compositions of both peptides were identical. Partial degradation by the dansyl-Edman method confirmed that the first six residues were the same as those determined for the skeletal peptide A, and from these data it was assumed that the sequences were identical (Table 1). The sequences of the two new peptides (B and C) were determined as shown in

Table 1. Amide assignments for peptide B were made as follows: after removal of Gly and Glu the mobility increased from 0.64 to 0.77 indicating that neutral residues had been eliminated; further degradation to give N-terminal Asp produced a non-radioactive tripeptide of mobility 0.52, confirming that the aspartic acid was charged. The mobility of peptide C at *p*H 6.5 showed that no amides were present. Thus the light chains of beef cardiac myosin contain three thiol sequences, one of which is identical to peptide A from skeletal "alkali" light chains.

The possibility remains that these three peptides do not derive from a single protein, since the light chains used in this experiment contained two components, of 27,000 and 20,000 daltons respectively[10]. Purification of a single component was achieved by chromatography of beef cardiac light chains before reaction with iodoacetic acid, on DEAE-cellulose (Whatman DE-52) in 50 mM tris-Cl at *p*H 8.0 with a gradient to 0.5 M KCl. Two peaks were obtained, the first of which gave a single major band on gel electrophoresis, while the second contained both proteins (Fig. 3 and ref. 19). Autoradiographs of digests of the two carboxymethylated fractions showed the same peptides in both fractions. The peptides were purified from the first fraction and amino-acid analysis confirmed the compositions of the three sequences (Table 1), showing that these three peptides derive from a single protein, whose mobility on gel electrophoresis corresponds to the 27,000 molecular weight light chain[10]. The presence of the same radioactive peptides in the second (mixed) light chain fraction may be accounted for in two ways: the counts may all arise from the contaminating 27,000 dalton protein or the smaller protein may contain some or all of the same thiol sequences. Measurement of the specific activities of the two fractions showed that the counts per mg in the first fraction were three times the value for the second fraction, which supports the hypothesis that the smaller protein contains fewer thiol groups. Further purification of the 20,000 dalton protein is essential before any sequence relationship can be investigated.

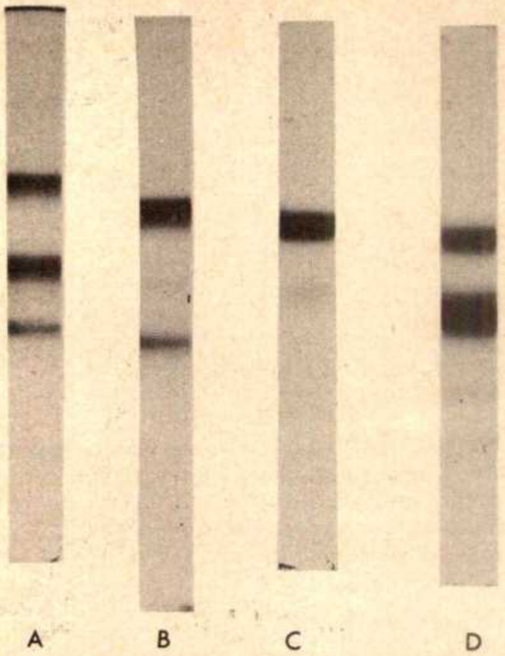

Fig. 3 Polyacrylamide gel electrophoresis of carboxymethylated light chains run on standard 7% acrylamide gels (*p*H 8.5) prepared according to the Canalco manual. *A*, Total light chains from chicken breast muscle myosin; *B*, "alkali" light chains from sheep leg muscle myosin; *C*, first peak fraction: beef cardiac myosin light chains; *D*, second peak fraction: beef cardiac myosin light chains.

Sheep Cardiac Light Chains

Light chains were dissociated from sheep cardiac myosin with 4 M urea, and reacted with ^{14}C-iodoacetic acid before digestion with chymotrypsin. The two dimensional electrophoretic separation of the peptides was similar to Fig. 2, and scintillation counting of the radioactive bands from the *p*H 6.5 electrophoretogram again showed approximately equal counts in each of the three major peptides (Fig. 1). The peptides were purified as before and amino-acid sequences determined (Table 1).

Thus both sheep and beef cardiac light chains are characterized by the same three thiol sequences, one of which seems to be identical to peptide A from rabbit "alkali" light chains[1], while the other two peptides do not resemble any of the known thiol sequences from rabbit myosin[20]. In an attempt to show that rabbit cardiac light chains are similar in their thiol peptides to beef and sheep light chains, cardiac myosin was prepared from 3 rabbit hearts, and the light chains dissociated

Table 1 Amino-acid Sequences of Thiol Peptides from Cardiac Myosin Light Chains

Peptide A													
Rabbit skeletal A:	Met–	Ala–	Gly–	Gln–	Glu–	Asp–	Ser–	Asn–	Gly–	CMC–	Ile–	Asn–	Tyr
Beef cardiac A:	⇀	⇀	⇀	⇀	⇀	⇀	—	—	—	—	—	—	—
Sheep cardiac A:	⇀	⇀	⇀	⇀	—	—	—	—	—	—	—	—	—
Peptide B													
Beef cardiac B:	Gly– ⇀	Gln– ⇀	CMC– ⇀	Gly– ⇀	Asp– ⇀	Val– ⇀	Leu ⇀						
Sheep cardiac B:	⇀	⇀	⇀	⇀	⇀	⇀	⇀						
Peptide C													
Beef cardiac C:	Asp– ⇀	Arg– ⇀	Thr– ⇀	Pro– ⇀	Lys– ⇀	CMC– ⇀	Glu– ⇀	Met– ⇀					
Sheep cardiac C:	⇀	—	—	—	—	—	—	—					
	T2 (⇀ ⇀) [0.0]			T4 (⇀ ⇀ ⇀) [−0.46]			T1 (⇀ ⇀ ⇀) [1.05]						
		T3 (⇀ ⇀ ⇀ ⇀ —) [−0.33]											

Amino-acid sequence data for chymotryptic peptides. —, Quantitative amino-acid analysis; ⇀, sequences determined by the dansyl–Edman method[16]; T1, T2 and so on denote tryptic digestion products, with the mobilities at *p*H 6.5 given in brackets underneath the sequence.

Table 2 Amino-acid Sequences of Thiol Peptides from Skeletal Myosin Light Chains

DTNB–light chains	
Rabbit 1:	Thr–Thr–Gln–CMC–Asp–Arg–Phe
Sheep 1:	⇀ ⇀ ⇀ ⇀ ⇀ ⇀ ⇀
Rabbit 2:	Lys–Asn–Ile–CMC–Tyr
Sheep 2:	⇀ ⇀ ⇀ ⇀ ⇀
"Alkali" light chains	
Rabbit A:	Met–Ala–Gly–Gln–Glu–Asp–Ser–Asn–Gly–CMC–Ile–Asn–Tyr
Sheep A:	⇀ — — — — — — — — — — — —

Amino-acid sequence data for chymotryptic peptides. —, Quantitative amino-acid analysis; ⇀, sequences determined by the dansyl–Edman method[16]; the amide assignments in this Table were determined for the rabbit light chain peptides[2].

and reacted with ^{14}C-iodoacetic acid. Autoradiography of the two dimensional electrophoretic separation gave a pattern of spots similar to Fig. 2. The absence of species differences in the thiol sequences was confirmed by analysis of the thiol peptides from sheep skeletal muscle myosin.

Sheep Skeletal Light Chains

Both DTNB and "alkali" light chains were prepared from sheep leg muscle myosin, and chymotryptic digests of the carboxymethylated proteins fractionated by electrophoresis at *p*H 6.5. Autoradiographs showed that the DTNB-light chains contained two major peptides, while the "alkali" light chains gave a single major band (Fig. 1). Peptides 1 and 2 from the DTNB-light chains and peptides A and A′ from the "alkali" light chains were purified and amino-acid compositions determined. These were identical to the equivalent peptides from rabbit light chains, but the sequences were determined for peptides 1 and 2 to confirm the identity (Table 2).

Table 3 Chemical Characteristics of Myosin Light Chains

Molecular weight *	Type of muscle	Thiol peptides †	Removal by DTNB
16,000	Skeletal	A	–
18,000	Skeletal	1, 2	+
20,000	Cardiac	—	–
25,000	Skeletal	A	–
27,000	Cardiac	A, B, C	–

* See preceding article[10].

† See Tables 1 and 2 for the thiol sequences of peptides A, B, C and 1, 2.

Comparison of the thiol sequences of light chains from cardiac and skeletal muscle myosins shows that peptide A from the "alkali" light chains of skeletal myosin is conserved in cardiac myosin, but striking differences are also evident (Table 3). The DTNB-light chains are associated only with skeletal myosin. Reaction of cardiac myosin with DTNB removes only traces of light chain material, and the thiol peptides characteristic of the DTNB-light chains (peptides 1 and 2) are absent from cardiac myosin. Structural differences between the light chains of cardiac and skeletal myosins are indicated by the presence of two additional thiol groups (peptides B and C) as well as the higher molecular weight of the larger cardiac light chain. These structural differences may account in part for the variation in ATPase activity between cardiac and skeletal myosins, although evidence also exists for structural heterogeneity in the heavy chains[15]. The extent of sequence homology between the two cardiac light chains remains unclear.

Similarities between cardiac myosin and myosin from slow skeletal muscle have been demonstrated by ATPase inactivation studies[21] and gel electrophoresis of the light chains[10,25]. Chicken anterior latissimus dorsi myosin gave two light chain bands identical in molecular weight to those from cardiac myosin, while red muscle from rabbit appeared to be mixed in that all five molecular weight components were present[10]. A preliminary investigation has been carried out with cat myosins to analyse the thiol peptides from fast twitch and slow twitch muscles. Myosin was prepared from flexor digitorum longus (fast twitch) and soleus muscles (slow twitch) whose homogeneity had been tested by examination of the contractile response[22]. The isolated light chains were reacted with ^{14}C-iodoacetic acid and chymotryptic digests prepared. Peptide purification showed that the fast muscle myosin contained both DTNB and "alkali" light chains, while the slow muscle myosin contained the three peptides characteristic of cardiac myosin (A. G. W., unpublished work). Thus the light chains of cardiac and slow-twitch muscles show similarities in their thiol sequences as well as in molecular weight. These results are consistent with the hypothesis that the light chains are involved in regulation of the contractile response[12,13,23,24].

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LETTERS TO NATURE

PHYSICAL SCIENCES

Internal Constitution of Mars

THERE are three basic hypotheses to account for the low density of Mars compared with the Earth. Ramsay[1] and Bullen[2] suggest that both planets have the same overall chemical composition, but that differential self-compression in their respective gravitational fields combined with phase changes lead to differing densities. This hypothesis implies that the Earth's core represents a phase transformation from the non-metallic state of the mantle to a denser metallic state. Jeffreys[3] and Urey[4] assume that Mars and Earth consist chiefly of silicates and metallic iron. The composition of each of these phases is similar in both planets but Mars contains a smaller proportion of metallic iron. A third hypothesis has been proposed by Ringwood[5,6], in which the relative abundances of the common metals, Fe, Mg, Al, Si and so on, are similar in Mars, Earth and Venus, and also similar to abundances in the Sun and in Type 1 carbonaceous chondrites. Differences in density between the planets are caused by differences in the amount of oxygen present, Mars being more oxidized than the Earth and Venus representing an intermediate state. Additional hypotheses on the constitution of Mars have been proposed[7-9] but these are essentially combinations of the second and third hypotheses mentioned above, and will not be considered further.

It now seems extremely improbable that the Earth's core represents a high pressure phase transformation of mantle material[10], and the first hypothesis may accordingly be dismissed. There are also difficulties associated with the second hypothesis. Urey has pointed out that the moment of inertia of Mars requires most of the metallic iron in Mars to be distributed throughout the mantle, with only a small proportion in a core. But MacDonald[11] has shown that if Mars contained the chondritic abundances of U, Th and K, extensive melting in the interior should have occurred over 4.5×10^9 yr, so that most or all of the iron should have segregated to form a core. A further difficulty is that the atmosphere of Mars contains a substantial amount of CO_2 and that water is also present. If the Martian mantle consists of a mixture of metallic iron and silicates, equilibrium considerations dictate that the volatiles which would be degassed into the atmosphere consist chiefly of CO and H_2 rather than CO_2 and H_2O (ref. 6). Moreover, the red colour of Mars suggests the presence of ferric iron which is not readily explained by the redox state implied by the second hypothesis[6].

In view of these difficulties we investigated the third hypothesis which maintains that Mars is composed of chondritic material in a higher state of oxidation than is displayed by the Earth or ordinary chondrites.

This investigation has been made possible by the measurement of the mean radius of Mars by the Mariner experiments and by planetary radar leading to determinations of the mean density and coefficient of moment of inertia, and by advances in our understanding of the role of phase transformations, not only within the Earth, but also in related compositions relevant to the Martian models[12]. The phase transformation behaviour of most of the minerals which may exist in Mars has been investigated experimentally at pressures up to 200 kbar, which corresponds to a range of depths including about 80% of the entire mass of the planet.

Table 1 Simplified * Composition of Type 1 Carbonaceous Chondrites

Component	Weight %
SiO_2	33.32
MgO	23.50
FeO	37.37
Al_2O_3	2.41
CaO	2.30
Na_2O	1.10

* All volatiles and sulphur omitted. Components present in amounts smaller than 0.5% omitted. NiO (1.9%) has been added to FeO. Iron is calculated as FeO, except that cases with varying proportions of iron calculated as Fe_2O_3 are considered in Table 2.

Table 2 Calculated Low Pressure Mineral Assemblages and Transition Pressures * for Oxidized Primitive Model Composition (Table 1) as Function of Oxidation State

Model	Fe^{3+}/ $Fe^{2+}+Fe^{3+}$ (atom %)	MgO/ MgO+FeO (mol. %)	Olivine (wt%)	Pyroxene (wt%)	Magnetite (wt%)	Trans. press. (kbar) (ref. Table 3)	
						A	B
I	67	100	20	40	40	151	262
II	35	68	60	19	21	135	229
III	5	54	94	—†	2	124	223

* Phase transitions A and B occur at pressures appropriate to a temperature–depth distribution with a uniform distribution of U, Th, and K throughout Mars in chondritic abundances[11].

† Other minerals—4%.

		Density increase (%)
Transition A		
Assumed to occur discontinuously at same depth	Olivine→spinel structure	10
	Forsterite→β-Mg_2SiO_4	8
	Pyroxene→garnet str.	10
Transition B		
Assumed to occur discontinuously at same depth	Spinel→Sr_2PbO_4 str.	9
	Mg pyroxenes→ilmenite str.	18
	(Mg garnet→ilmenite str.)	8
	Ca pyroxenes→perovskite str.	22
	(Ca garnet→perovskite str.)	12
	Magnetite→calcium ferrite str.	11

We take as our starting composition that of the metallic oxide components of Type 1 carbonaceous chondrites (Table 1) and have considered models having three different oxidation states, which result in different mineralogical compositions (Table 2). Model I is the most oxidized, all the iron occurring as magnetite, while the silicates are iron-free. Model II is an intermediate case, having about half of the iron present as FeO in solid solution in olivines and pyroxenes, and the remaining iron present as magnetite. This model has an oxidation state similar to the Karoonda chondrite[12] and mineralogically is the most plausible of those considered. Model III is the most reduced, containing a maximum of FeO and minimum of Fe_2O_3. In this model, calcium is present as the larnite molecule.

Each of these models would be expected to undergo a series of major phase transformations over the pressure range occurring within the Martian interior and because of the differing mineralogical compositions, the transition pressures and corresponding density changes differ for each model. Nevertheless, experimental phase transformation studies[12,14] strongly indicate that the relevant transformations for the models would dominantly occur in two stages, as in the Earth[15]. The first stage (transition A) is due to the transformation of olivine to the spinel or βMg_2SiO_4 structure and of pyroxene to the garnet structure. The second stage (transition B) consists of transformations of spinels and garnets to denser silicate polymorphs characterized by octahedral coordination of silicon and probably possessing Sr_2PbO_4, ilmenite, perovskite and related $CaFe_2O_4$ or $CaMn_2O_4$ structures[12,16-18]. Although transitions A and B would each occupy a substantial depth interval, we have simplified the models by assuming them to occur discontinuously at two characteristic pressures. The error introduced into subsequent calculations by this simplification is trivial. Our best estimates of the characteristic pressures for transitions A and B (at 1,000° C) based on the cited references are given in Table 3 together with estimates of the mean temperature gradients (dP/dT) of these transitions.

Table 3 Properties* of Principal Mineral Assemblages (Model II)

Assemblage	ρ_0 (g cm^{-3})	K_0 (kbar)	α_0	Characteristic transition pressure at 1,000° C (kbar)	$\frac{dP}{dT}$ (bar/° C)
Olivine, pyroxene magnetite	3.79	1,300	3.5×10^{-5}		
Transition A	—	—	—	105	30
Spinel garnet magnetite	4.06	1,900	2.9×10^{-5}		
Transition B	—	—	—	200	20
Post-spinel† assemblage	4.50	2,300	3.0×10^{-5}		
High pressure form of magnetite‡	5.82	2,200	3.0×10^{-5}	200	20

* ρ_0 = zero pressure density, K_0 = zero pressure bulk modulus. α_0 = zero pressure coefficient of thermal expansion at 1,000° C.

† Post-spinel assemblage consists of high pressure polymorphs with ilmenite, Sr_2PbO_4, perovskite and calcium ferrite type structures.

‡ High pressure form of magnetite believed to have structure related to that of calcium ferrite or calcium manganite[1,12,16-18,21].

As our models are based in the first instance on chondritic compositions, it is appropriate to use the chondritic U, Th and K abundances in estimating the internal temperature distribution within Mars. The relevant thermal models have been calculated by MacDonald[11]. We have used a temperature distribution shown in his Fig. 19 ($\varepsilon = 10$ cm^{-1}) in our calculations. For a wide range of initial assumptions about boundary conditions, there is little difference between MacDonald's models in the outer 800 km of Mars which accounts for most of the mass and moment of inertia. Thus our subsequent calculations are not sensitively dependent on thermal considerations, provided chondritic abundances are used. Using the chondritic temperature–depth relationship, the parameters of transitions A and B (Table 3) and pressure–depth relationships which are obtained subsequently, the depths at which transitions A and B occur within Mars according to models I, II and III are fixed. These are given in Table 2.

We now have three models giving the mineralogy as a function of depth and wish to determine the density and pressure distribution throughout Mars for each of these models. The principal physical properties required are the zero-pressure densities, bulk moduli and thermal expansions of each mineral assemblage. The zero-pressure density ρ_0 is the decisive property and can be accurately estimated for each assemblage from the densities of individual minerals determined either directly or indirectly[12,14,19-21] combined with the relative proportions of individual minerals dictated by the particular compositional model. The zero-pressure bulk modulus (K_0) can be obtained with adequate precision by a combination of direct measurements on minerals and isostructural analogue compounds or alternatively using the seismic equation of state[12,16,19,21]. Results obtained from the use of both methods are in good agreement. The thermal expansion (α_0) coefficients used are based on direct measurements on minerals and related isostructural analogue compounds[19]. The values of ρ_0, K_0 and α_0 estimated in this way for each of the low pressure, intermediate pressure and high pressure mineral assemblages for model II are given in Table 3. Corresponding physical properties for the other models have been estimated similarly.

The density and pressure distributions throughout Mars for each model were then calculated, following the methods applied to the Earth's mantle by Clark and Ringwood[22].

The isothermal pressure–density relation is taken to be the second-order Birch-Murnaghan equation of state[23]

$$P = 3K_0\left[\left(\frac{\rho}{\rho_0}\right)^{7/3} - \left(\frac{\rho}{\rho_0}\right)^{5/3}\right]$$

Densities were further corrected for expansion from 0° C to the chosen chondritic temperature distribution. The thermal expansion coefficient was taken to be independent of temperature and to vary with pressure according to the relation[22,23]

$$\alpha/\alpha_0 = 1 - \frac{4P}{K}$$

The calculation proceeds inwards from the surface in steps. The pressure–depth relation is calculated for the model under consideration by an iterative procedure, yielding the density–depth relation. Mass and moment of inertia are then found by quadrature. The mean density of Mars thus obtained for each model and the corresponding moment of inertia coefficient, I/MR^2, are given in Table 4.

Table 4 Mars : Model Densities and Moment of Inertia Coefficients

Model	Mean density	$\frac{I}{MR^2}$
I	3.921	0.392
II	3.972	0.391
III	3.991	0.391
IIA*	3.942	0.377
IIB†	3.942	0.373
Mars—(observed)	3.942 ± 0.005	0.377 ± 0.004

* Model IIA has differentiated crust 195 km thick with density of 3.0 g cm^{-3}.

† Model IIB has differentiated core of HPP magnetite with radius of 1,638 km.

The mean densities of all three models are in close agreement with the observed density of Mars. Exact agreement could readily be obtained for models II and III by minor alterations of these models well within the uncertainty limits, but model I appears to be too light, in spite of the fact that it agrees better with the observed density than do the other models. The increase in density at transition A must be greater than seems to be allowed by the mineralogy in order to raise the mean density to the observed figure.

The moment of inertia coefficients for all models are substantially higher than the observed value. The increase of density with depth in Mars is thus substantially greater on the average than in the models. In order to achieve compatibility, the models must be amended to incorporate the effects of internal differentiation. Two differentiated models were considered. In the first (model IIA) a crust of density 3.0 g cm^{-3} is assumed to have differentiated from the Martian mantle. In order to yield a moment of inertia coefficient of 0.377, the thickness of this crust on models II and III must be about 200 km, and small compensating density changes throughout the mantle must be assumed. A differentiated crust of this thickness appears excessive, although the possibility cannot be entirely eliminated. The second differentiated model assumes that the magnetite has segregated to form a core, analogous to the metallic core of the Earth. In model IIB, the magnetite in model II is differentiated to form a core with a radius of 1,638 km representing 21% of the mass of Mars. The magnetite is assumed to be present as the high pressure polymorph[12,16–18,21] (HPP). Differentiation of a magnetite core according to this model eliminates the region occupied by the "post-spinel" assemblage below discontinuity B of models I, II and III. The moment of inertia coefficient is 0.373 which is slightly smaller than the best coefficient (0.377), although within its estimated error. Obviously, the assumption of a slightly smaller degree of differentiation could produce an I/MR^2 of 0.377. There is insufficient magnetite in model III to produce a large enough core to provide the correct moment of inertia coefficient. Accordingly, this extreme model can also be dismissed.

We conclude that a differentiated oxidized chondritic model can indeed provide the observed density and moment of inertia of Mars (Fig. 1). There is a range of possible models within this category. If differentiation has proceeded sufficiently to produce a core, it seems likely that a crust may also be present. Thus the most probable model would represent a combination of models IIA and IIB. This would still leave some magnetite in the mantle. To avoid the implication that only partial segregation of magnetite into the core had occurred, a variant of model IIAB towards model III might be assumed. This would imply a somewhat lower $Fe^{3+}/Fe^{2+}+Fe^{3+}$ ratio than model IIAA and, consequently, a correspondingly smaller total amount of magnetite.

Another model tested assumed that the HPP magnetite core of IIB was entirely replaced by a troilite core (necessarily molten for chondritic U, Th and K abundances). This model provided the correct moment of inertia, but its density was too low. Nevertheless, it appears likely that some troilite would be permitted in a cosmochemically realistic model. Thus, the Karoonda chondrite[13] contains about four per cent of (Fe,Ni)S. This is permitted within the range of possible differentiated variants of model II. It is also likely that a small metallic iron core[9,24] would be permitted within the framework set by our overall boundary conditions—density, moment of inertia, chondritic abundances and variable redox state. But the presence of an iron core is not readily reconciled with the inferred oxidized state of surface rocks and atmospheric composition.

It is interesting that neither of the extreme class I or III models was satisfactory, while a range of models derived from differentiated versions of model II were satisfactory. It happens that model II representing an intermediate oxidation state similar to that displayed by the chondrite "Karoonda"[13] is also the most reasonable one from a chemical and mineralogical viewpoint.

We have concluded that if Mars has an oxidized chondritic composition, then necessarily it must be a highly differentiated body, most probably possessing both a large core dominantly of HPP magnetite and a crust. It is satisfying that this conclusion is concordant with thermal history considerations. If Mars has the chondritic abundances of U, Th and K, the radioactive heat generated over 4.5 billion yr inevitably would have caused extensive internal melting and differentiation[11]. Moreover the comparative dearth of craters on the Hellas region[25] indicates the occurrence of some dynamic crater obliteration process, indicating an "active" planet and perhaps suggesting currently active magmatism and differentiation. Our model is also consistent with the absence of a magnetic field on Mars, because the presence of a large, electrically conducting and convecting liquid core is not presumed.

Our work shows that the properties of Mars are consistent with an overall oxidized chondritic composition, in which, moreover, the relative abundances of metals are believed to be similar to those in the Sun. Self-consistent models of Earth and Venus can also be derived from chondritic or solar abundances, employing oxidation state as the major compositional variable[5,6,12]. The postulate that mean oxidation states may vary between planets is inherently plausible. Chondritic meteorites themselves display a wide range of oxidation states. Important differences in oxidation states between lunar and terrestrial basalts and between their respective source regions have also been demonstrated. Finally, from a consideration of chemical processes occurring during the formation of planets, it is easy to understand how differences in mean oxidation states of planets might arise. Indeed, recent theories of planet formation[6,26–28] which differ in important respects nevertheless have one aspect in common: they imply that it would be somewhat miraculous if all planets had acquired the same mean oxidation state.

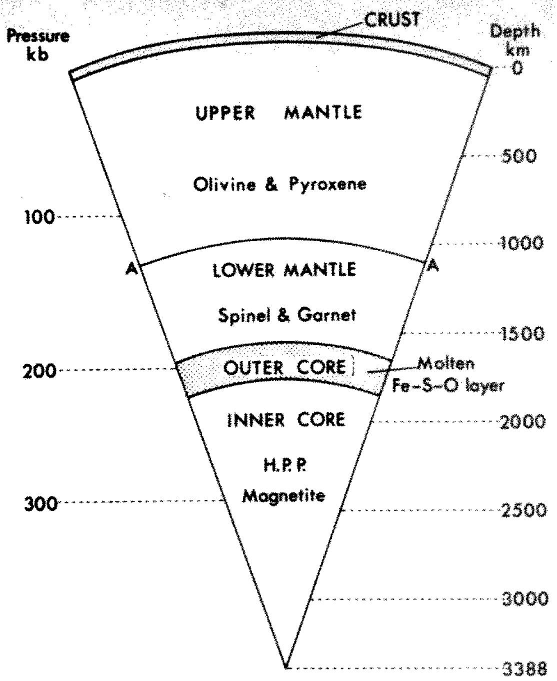

Fig. 1 Hypothetical section through Mars based on a variation of model IIB.

Our hypothesis has the advantage that it is not necessary to make *ad hoc* postulates about the occurrence of metal–silicate fractionation in the solar nebula prior to planetary accretion by mechanisms which are poorly understood and for which no direct evidence exists. In contrast, the present redox hypothesis invokes a process which is known to have operated during planetary formation and which invokes relatively simple and well understood chemical equilibria.

In view of the imminent missions to investigate the surface composition of Mars it is worthwhile asking what predictions might be made on the basis of the two hypotheses discussed above. The redox hypothesis implies an overall chondritic composition for the planet. The K/U and Na/Ca ratios of surface igneous rocks would accordingly be expected to be much higher than occur, for example, in corresponding terrestrial and lunar rocks. On the alternative hypothesis that Mars consists of a mixture of metallic iron with silicates similar to those in the Earth's mantle, the K/U and Na/Ca ratios would be expected to be close to the terrestrial values. According to this latter hypothesis, metallic iron should be an important component of Martian rocks whereas on the redox hypothesis, metallic iron would be absent, and Martian rocks would be highly oxidized. The most important difference is that on the redox hypothesis strong differentiation of the planet would be expected, leading to a chemically and petrologically heterogeneous outer crust together with a dense core mainly of oxides. On the metal–silicate mixture hypothesis, internal heating by

K, U and Th has been insufficient to cause extensive differentiation, so that most of the iron has remained in the mantle.

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Plutonium Content of Soil at Nagasaki

THE explosion of a plutonium atomic bomb over Nagasaki city in Japan took place at 1100 h on August 9, 1945. The bomb was detonated at a height of about 500 m above the place indicated in Fig. 1; the direction of the wind was from the west. In July 1969, samples of surface soils (each 10 cm deep) were taken from the less disturbed surface of the ground, such as graveyards or grassland, so that the amount of plutonium remaining in the soil after 24 yr could be determined. The sampling locations are shown in Fig. 1; three different samples (N1, N2, N3) were taken from Nishiyama area where high radioactivities due to fission products had been detected after the explosion The contour of the radioactivity dose rate in air in the autumn of 1945 is shown in Fig. 2.

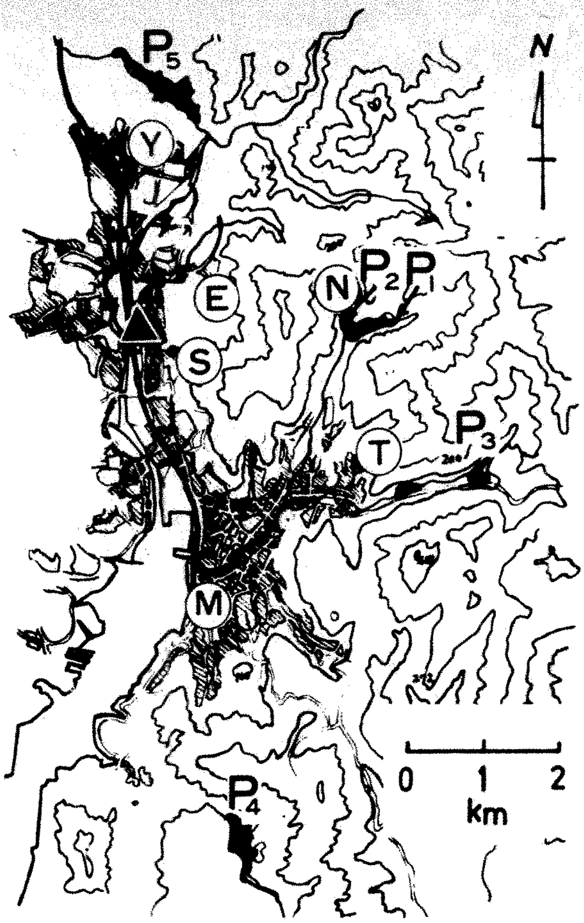

Fig. 1 Sampling locations of soils in Nagasaki. ▲, Centre of atomic bomb explosion; *Y*, Ieno-chō; *E*, Ehira-chō; *S*, Sakamoto-chō; *M*, Minamiyamate-chō; *N*, Nishiyama-chō; *T*, Narutaki-chō.

The powdered dry soil samples (~ 10 to 50 g according to the plutonium content) were treated with 8 M nitric acid after adding ^{236}Pu tracer prepared by the reaction ^{237}Np (γ, n) $^{236}\mathrm{Np} \xrightarrow{\beta^-} {}^{236}\mathrm{Pu}$ (ref. 1). Ferric hydroxide co-precipitation was then induced from this sample solution in the presence of carbonate ion, followed by the dissolution in 8 M HNO_3 and solvent extraction with trioctylamine. This method had been

Table 1 Plutonium Contents of Soils from Nagasaki

Sample Location*	Sign	^{239}Pu		^{238}Pu	^{238}Pu/^{239}Pu	^{90}Sr
		(pCi kg^{-1})	(mCi km^{-2})	(pCi kg^{-1})	(activity ratio)	(pCi kg^{-1})
Ieno (1.6 km)	Y	22 ± 2	~1	7 ± 1	0.3 ± 0.05	324 ± 31
Ehira (1.1 km)	E	68 ± 4	~5	15 ± 2	0.2 ± 0.02	740 ± 40
Nishiyama (2.8 km)	N1	190 ± 8	~15	12 ± 1	0.06 ± 0.005	609 ± 39
	N2	473 ± 28	~38	43 ± 3	0.09 ± 0.009	794 ± 58
	N3	246 ± 12	~19	29 ± 3	0.11 ± 0.01	841 ± 55
Sakamoto (0.8 km)	S	76 ± 4	~6	20 ± 2	0.2 ± 0.02	968 ± 66
Narutaki (3.6 km)	T	46 ± 3	~4	(22 ± 2)	(0.4 ± 0.04)	988 ± 58
Minamiyamate (4.4 km)	M	23 ± 2	~2	—	—	214 ± 22

* Distance from the centre of the atomic bomb explosion.

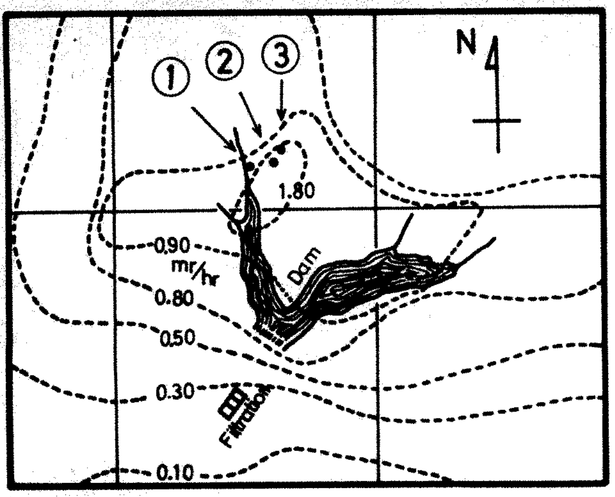

Fig. 2 Sampling points at Nishiyama area and the contour of radiation dose in the autumn of 1945.

proposed in our previous study[2] and some details were described in that article. The final determination of plutonium isotopes was made by α-ray spectrometry of an electrodeposited counting source, using a double gridded ionization chamber as detector. The α-spectrum from the sample (N3) of Nishiyama area is shown in Fig. 3 as an example.

Our determinations of the ^{239}Pu and ^{238}Pu contents are summarized in Table 1, together with the ^{90}Sr contents of these samples determined by the Japan Analytical Chemical Research Institute. It is remarkable that the ^{239}Pu contents at Nishiyama are still very high compared with the general level[2,3] of this nuclide, even after 24 yr, although the contents of ^{90}Sr are not very different and are of the same order as the content of other soil samples (10 cm depth) in Japan[2]. These facts may be due to differences in retention ability of the ground for various elements and are consistent with the experimental data[4] obtained by radiotracer. The amount of ^{239}Pu per km^2 calculated from these data shows that the plutonium content of the sample N2 is about ten times higher than the plutonium content in other surface soil samples ($\sim$1–3 mCi/km^2) due to long-range fallout from subsequent nuclear test explosions[2,3]. For the purposes of a discussion of the ratio ^{238}Pu/^{239}Pu, it must be recalled that some ^{238}Pu was added recently during the burn-up in 1964 of the SNAP-9A satellite which used ^{238}Pu as an auxiliary power source.

These results can be compared with the data[5] from the soils of New Mexico which were subjected to the plutonium atomic bomb test of July 16, 1945. In 1956, an activity of about 24 d.p.m. ^{239}Pu g^{-1} soil was still found at a point 28 miles from the test centre.

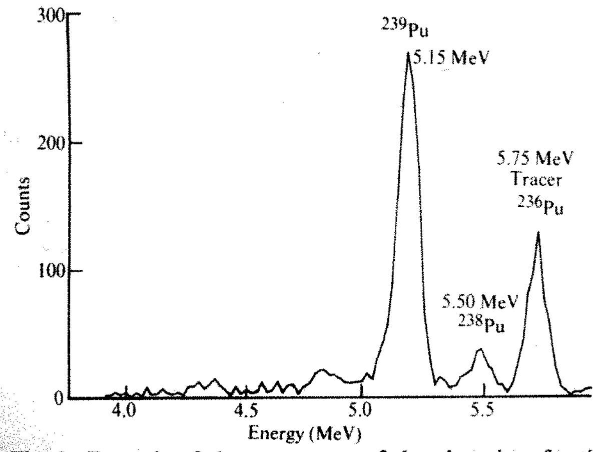

Fig. 3 Example of the α-spectrum of the plutonium fraction from sample N3. Sample weight, 10.2 g; chemical yield, 36%; measuring time, 1,450 min.

Further studies of plutonium remaining in Nagasaki have been made by the new method on the samples (P_1 to P_5) taken from the bottoms of four water reservoirs shown in Fig. 1 and have been reported elsewhere[6].

These results may be important for the future studies of environmental radioactivity because they show that plutonium contaminants in soil are not easily removed naturally.

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Chrysotile Asbestos in Urban Air

THE industrial use of chrysotile asbestos is increasing and the question of whether its concentration in urban air constitutes a hazard has been raised. But measurements of asbestos in air near asbestos factories have proved negative with present analytical methods, so under the sponsorship of the Asbestosis Research Council we are developing a more sensitive technique. This article is a preliminary account of the estimation of chrysotile near a large asbestos textile factory at Rochdale, Lancashire. There are several uncertainties in the technique, so we were expecting to obtain only an order of magnitude estimate. Nevertheless this would have been an important figure to have because of the lack of data on the amount of asbestos in air. As it happened, we were only able to determine an upper limit for the chrysotile concentration which turned out to be three orders of magnitude lower than the threshold value for occupational exposure set by asbestos regulations. Obviously even more sensitive techniques are required and are now being developed.

We used an X-ray diffraction technique based on the measurement of the integrated area under the (002) peak of chrysotile. The equipment, which consisted of a Phillips 1010 generator, a vertical goniometer with a step scanning attachment, and a proportional counter with pulse height discrimination, could be reliably calibrated down to 10 µg of chrysotile compared with the 1 to 10 mg range reported by Crable[1], and was cross-checked by estimating the magnesium content of the calibration samples by atomic absorption spectroscopy. Sampling involved the collection of airborne solids from 1,000 m^3 (10^6 l.) of air by an electrostatic device (H. Litton Systems Inc.) in which up to 10,000 l. min^{-1} are drawn through a 20 kV corona discharge. Particles in the air are electrostatically precipitated onto a plate and concentrated into $\sim$100 ml. of liquid.

The collection efficiency depends on the size distribution of the particles and the sampling rate, but the size distribution of chrysotile in the atmosphere is not known. Therefore we estimated the collection efficiency indirectly by running the sampler in part of the asbestos factory where a low concentration of asbestos is known to occur (Fig. 1) and we found the collection efficiency to be almost 100% when the air is sampled at about 2,000 l. min^{-1}, dropping to between 25 and 50% at the rate of 10,000 l. min^{-1}, depending on the actual size distribution present. As we were aiming at only an order of magni-

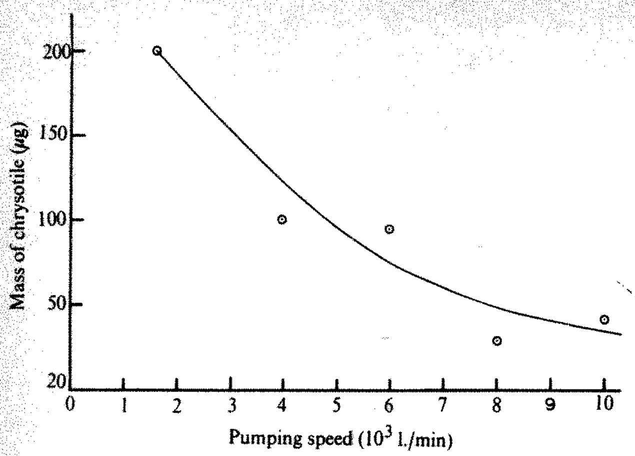

Fig. 1 Observed amounts of chrysotile in 5,000 l. of factory air, sampled at different rates.

Table 1 Weather Conditions during Sampling

Date (1970)	Site	Wind	Weather
April 22	1	SW moderate	Broken cloud
April 24	1	SW slight	Ground haze
April 27	1	NE moderate	Ground haze
April 29	1	SW moderate	Ground haze
May 6	1	S strong	Ground haze
May 13	1	N fresh	Ground haze
May 28	3	W light	Overcast, dull
May 28	3	W light	Overcast, dull
May 30	4	W light	Overcast, dull
May 30	4	W light	Overcast, dull
June 3	2	SW light	Overcast
June 10	2	SW slight	Heat haze
June 10	2	SW slight	Heat haze
October 23	1	W moderate	Broken cloud
October 23	1	W moderate	Broken cloud
October 23	1	W moderate	Broken cloud
October 28	1	N light	Broken cloud
October 28	1	N light	Broken cloud
October 28	1	N light	Broken cloud

tude assessment of asbestos in urban air, we were prepared to accept this uncertainty in the collection efficiency.

The map (Fig. 2) and Table 1 show the location of the sampling sites and the conditions in which the samples were obtained. The factory is in a hollow, and sampling site No. 2 is at the same height as the roof of the filter gallery, which is the chief air outlet from the factory. Sampling site No. 1 is about 30 foot higher than site No. 2. Sites 3 and 4 were in the gardens of houses, site 3 being about 5 km upwind of the factory and site 4 being about 300 m downwind.

All the diffraction traces (for example, Fig. 3) contained strong lines of kaolinite and quartz, probably from the local soil, which made the assessment of chrysotile difficult because the broad (001) line of kaolinite (7.18 Å) is close to the major (002) line of chrysotile (7.36 Å). Fortunately chrysotile is easily decomposed by boiling in 1 N hydrochloric acid whereas kaolinite is unaffected, so it should be possible to measure the amount of chrysotile present by subjecting the samples to acid leaching and measuring the corresponding reduction of the intensity of the composite X-ray band. The fact that this process led to no reductions in band intensity for any of the samples indicated that the amount of chrysotile present was below our detection limit.

We ought to have been able to detect 10 μg of chrysotile by itself, but clearly the presence of kaolinite may have reduced the sensitivity. But the addition of 100 μg of chrysotile to our collected samples could easily be detected, so we can say that our samples collected from 1,000 m^3 of air contained less than 100 μg of chrysotile—in other words, there was less than 0.1 μg of chrysotile per m^3 of air. The threshold limit for occupational exposure set by the 1969 Asbestos Regulations[2] is 0.1 mg m^{-3}.

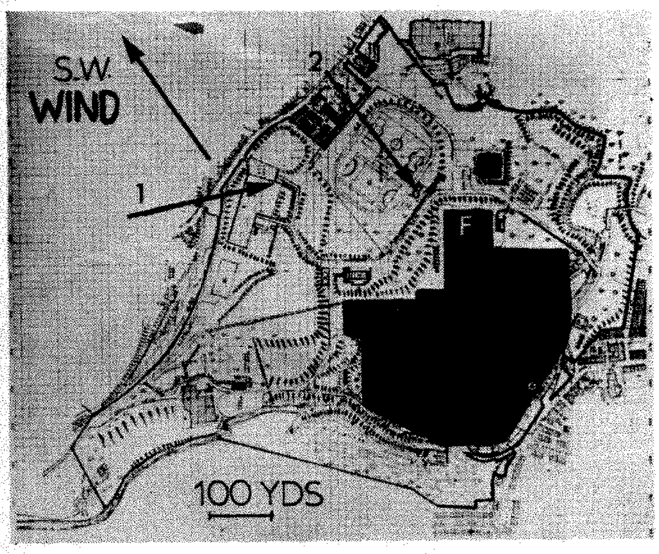

Fig. 2 Plan of T.B.A. factory, Rochdale. The sampling sites are indicated by the arrows 1 and 2. *F*, Position of the chief filter gallery exhausts.

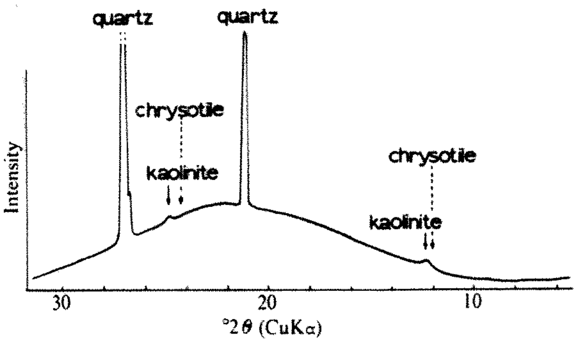

Fig. 3 X-ray diffraction pattern from a typical dust sample near the Rochdale factory.

A more sensitive method for estimating chrysotile is required, and we are developing a technique based on electron microscopy. Preliminary examinations under the electron microscope of samples collected by the Litton sampler indicate that the actual chrysotile level may be a further three orders of magnitude below the X-ray detection limit (that is, about 0.1 ng).

The samples have so far been collected in the close vicinity of the Rochdale factory. It is now proposed to sample air at certain representative urban and rural locations in UK and estimate their chrysotile content.

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Post-occultation Reception of Lunar Ship Endeavour Radio Transmission

The reception of radio signals from the orbiting lunar spaceship Endeavour after its occultation behind the lunar limb seems to confirm in part a previous suggestion[1]. Similar observations arranged with the lunar command module during the Apollo 14 mission were unsuccessful because of interference from local emissions.

The transmitter normally used for communication between the lunar command module and the lunar landing party was turned on continuously during a period of lunar orbiting between 0026 and 0132 EST, August 3, 1971. The frequency of this transmission was 259.7 MHz with a steady square-wave modulation at 31.6 kHz. This transmission was received by a special receiver using the Air Force Cambridge Laboratory 150 foot radio telescope as an antenna. This radio telescope is located at Sagamore Hill near Hamilton, Massachusetts, USA (latitude 42°, 37′, 55.6″ N and longitude 70°, 49′, 04.5″ W).

The turning on of the spacecraft transmitter was delayed for several hours from the planned time because of astronaut activity required to ensure satisfactory air seals after the return of the lunar landing party. By the time turn-on was achieved, the Moon was so near to setting, as observed from Sagamore Hill, that unfortunately only one observation could be made.

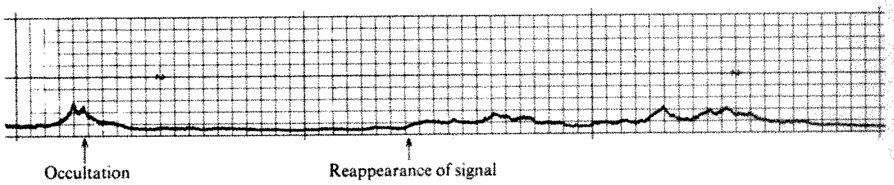

Fig. 1 Record of receiver response (1 division = 5 s).

The interference encountered during the previous mission was not present during this observation, so that the receiver noise level was reduced from about 35 mV on the receiver output to about 2 mV. This improved sensitivity as compared with that of the Apollo 14 test allowed an excellent observation of the occultation of the spacecraft and the signal as the Endeavour transmitter moved behind the edge of the Moon. The signal reappeared 115 s later with an intensity many times the noise level (peaking to about 15 mV) and remained discernible for about 140 s. The reception is shown on the accompanying photograph of the pen-recorded strip chart (Fig. 1). Records were also taken by means of magnetic tape and digital sampling of receiver output voltage. The signal was further observed visually on an oscilloscope, and the characteristic modulation could be clearly seen both before and after occultation.

The height of the Endeavour's orbit above the lunar surface was about 108 km at the time of occultation and was reasonably uniform thereafter. Thus, the Moon ship passed along about 25° of its orbit as measured from the lunar centre during the period between the time that the radius vector from the ship to the lunar centre came perpendicular to the direction toward the Earth and the time of occultation. This represents about 960 km on the lunar surface directly below the Endeavour's orbit. During the 115 s that elapsed between occultation and reappearance of the signal, the ship passed over an additional 177 km of the lunar surface; then, during the renewed signal, the ship passed through 7° more of orbit, or a lunar surface distance of 215 km. Projected on the Earth's direction vector (which does not lie in the plane of orbit, because of the inclination necessary to ensure that the orbit would pass over the relatively northern landing site), this progress is measured by 175 km on the lunar surface.

The surface distance passed over between occultation and the return of the signal when projected on the line of signal is about 135 km. This distance places the Endeavour transmitter 63 km below the point where the Earth line of sight is tangent to the lunar surface. At the time when the signal finally ended, the "line of sight" from the Earth to the Endeavour passed about 158 km beyond the limb of the Moon. The librations of the Moon were all small at the time of these observations and the relatively insignificant corrections for these librations have been included in these figures.

Several possibilities for explaining these results may be considered. The passage of a refracted wave through the bulge of the Moon, as suggested for much longer wavelengths in previous articles[1,2], seems unlikely because the small refraction angles indicated would require much too small a refractive index for the lunar surface material. Also, the Moon is rather rough in terms of this short wavelength and the attenuation for such a high frequency is much too high, as indicated by measurements of returned lunar material[3]. The possible existence of a temporary ionosphere produced by gas emissions from the spacecraft appears to be unlikely because of the large amount of material required for the necessary deflexion of such high-frequency waves (259.7 MHz).

The most probable explanation seems to be one of two possibilities. First, the signal was received from a surface wave carried around the Moon, in a way similar to the propagation of waves in the broadcast band on the Earth's surface[4,5]. This explanation appears possible because of the extreme dryness of the Moon and the low electrical conductivity of lunar surface material, as compared with seawater and to soil containing considerable ground water on the Earth. Second, the signal was received from the prismatic refraction of mountain formations in this part of the Moon, where paths through lunar material may be relatively short and the materials may have properties differing somewhat from the average. Work is proceeding to determine, if possible, which is more likely. It is hoped that a repeat test during the Apollo 16 mission can be arranged and that observations can be made for several orbits of the command module. It is also expected that observations during future lunar missions will make possible more definitive data on the radio-frequency properties of the lunar surface, at much longer wavelengths, which will also be important tools in exploring the interior of the Moon.

We thank the Air Force Cambridge Research Laboratory for the use of their 150 foot radio telescope and Dr Jules Aarons and the operators for their assistance. We thank Dr Edward Lilley and Mr Hayes Penfield, of Harvard College Observatory, for the use of their receiver and for many discussions. We also should like to express our appreciation to NASA and the crew of Apollo 15 for their cooperation.

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Statistical Mechanics and the Critically Branched State

THIS communication deals with controversies concerning a standard reference case for equilibria in polymer science, namely the equilibrium distribution for a random f-functional polycondensation system. On the assumption that all functionalities are equally reactive and that intramolecular reaction does not occur, this distribution was derived by different probability arguments by Flory[1,2], Stockmayer[3], Good[4], Whittle[5] and others:

$$w_x = \frac{(fx - x)!\,f}{(fx - 2x + 2)!\,(x - 1)!}\,(1 - \alpha)^{fx-2x+2}\,\alpha^{x-1} \quad (1)$$

where w_x is the weight fraction of x-mer and α the conversion. Recently, Masson *et al.*[6] have claimed that Flory's derivation contains logical errors in the use of *a priori* probability and have denied that certain probabilistic operations used by Flory were meaningful. From an amended probability argument, they derived a new distribution which in the same notation takes the form

$$w_x = \frac{(fx - x)!}{(fx - 2x + 1)!\,(x - 1)!} \left(1 - \frac{\alpha f}{2(f - 1)}\right)^{fx-2x+1} \left(\frac{\alpha f}{2(f - 1)}\right)^{x-1} \left(1 - \frac{\alpha f}{2}\right) \quad (2)$$

Distributions (1) and (2) are both normalized and share the same number average $DP_n = \langle x^{-1}\rangle^{-1}$. Distribution (1), however, describes correctly the unique dimerization equilibrium for $f = 1$, whereas distribution (2) obviously does not. Moreover, distributions (1) and (2) differ vitally as regards the weight average ($DP_w = \langle x\rangle$), which diverges for distribution (1) at

$$\alpha_c = 1/(f - 1) \quad (3)$$

This divergence was interpreted by Flory as the statistical basis of gelation at the gel point α_c. The behaviour of matter in the critically branched state, that is, of systems near their gel point, has been rationalized on this basis. For instance, sol–gel analysis[7] accounts for measurements on many different systems.

The distribution of Masson *et al.* has a mean (DP_w) which does not diverge until α attains the value $2/f$, where the DP_n of both distributions diverges also. This point is the limiting conversion possible for a strictly tree-like gel (that is, one free from rings) and Bruneau[8] has also sought to identify this point with experimentally observed gel points, thus implicitly denying the validity of sol–gel analysis. Masson has adduced experimental results in support of distribution (2) from measurements of equilibrium monomer concentrations in ionic polysilicate melts.

There are two methods of settling the controversies unequivocally. The first method examines the mutually contradictory arguments of various authors, all of which are based on probability theory, and removes the erroneous arguments by the only procedure valid in deductive science. That is, an axiomatic basis is defined for probability theory, and it is then shown which statements of any author are inconsistent with the defined axioms. (The history of the axiomatics of probability theory has itself been rife with controversy. Some problems in probability theory have different solutions according to the set of axioms adopted.) Great care has been taken by mathematicians to define various possible axiomatic bases of probability theory which appeal to them. Not without reason, large initial sections of texts on probability theory (that of Renyi[9], for example) are taken up by this subject. The controversies surrounding polycondensation and gelation, though not lacking in power of rhetorical exposition, are too far from such a standard of rigour or from an agreed axiomatic basis for the first method of settling them to be applied with any confidence.

The second method, which is therefore preferable and is adopted here, derives the correct answer afresh from statistical mechanics without probability arguments. It is important to make clear the rationale of this method. Statistical mechanics is actually the relevant universal discipline for calculating equilibrium distribution of molecules. Any other direct probability argument is to be regarded as of an *ad hoc* nature. Of course, statistical mechanics is itself founded on axioms which include probabilistic ones. Several very distinct sets of axioms for statistical mechanics have been examined in detail, ranging from the classical work of Fowler and Guggenheim[10] to the modern and elegant treatment by Penrose[11]. Such works have succeeded in deriving identical molecular partition functions from different sets of premises. These partition functions allow molecular distributions to be calculated by routine methods free from probability theory and from the need to question the axiomatic foundations in each individual instance. Such partition functions have not so far shown the axiomatic foundations to be at variance with their application to the physical world. On the contrary, they are supported by an impressive body of thermodynamic and spectroscopic measurements. Thus the second method of settling the controversy works upward from a level (partition functions) above which probability theory and *ad hoc* arguments are no longer required, whereas at a deeper, axiomatic level the status of partition functions has been secured by extensive work by mathematicians. The calculation of random ring-free f-functional polycondensation equilibria from partition functions for linear or non-linear polyatomic molecules (for example, ref. 10, equation 329, 2) is essentially of a routine nature. The translational factors of the partition functions are not relevant to condensed polymer systems and are omitted. The relevant factors are the rotational symmetry numbers. Provided there is free rotation of the bonds between repeat units, the symmetry number of the jth isomer in the x-mer fraction is proportional to the order $|G_{xj}|$ of the symmetry group (automorphism group[12]) of its molecular graph. Indeed the form of the equilibrium distribution of a polycondensate is not affected if all the species present are taken in their completely floppy ("graph-like") states[13]. The combinatorial entropy change of the reaction

$$x\mathrm{M} \rightarrow \mathrm{P}_{xj} \qquad j = 1, 2, \ldots \quad (4)$$

is then derived from the partition functions, namely

$$\Delta S_c = R \ln |G_\mathrm{M}|^x / |G_{xj}| \quad (5)$$

where M denotes monomer and P_{xj} the jth x-mer in the polymer distribution. The equilibrium constant of reaction (4) is

$$K_{xj} = w_{xj}/w_1{}^x N^{x-1} x \quad (6)$$

where N is the total concentration of repeat units, and w_{xj} the weight fraction of the jth x-mer. As proved from statistical mechanics by Gordon and Temple[13], any phenomenological equilibrium constant can be factorized into two factors, one combinatorial and one reflecting fundamental driving forces. Absence of intramolecular reactions implies that every x-mer has $(x - 1)$ inter-unit bonds, and equireactivity of functionalities shows that each of these bonds has the same fundamental entropy ΔS_b and enthalpy ΔH_b of formations

$$K_{xj} = (\exp \Delta S_c/R) K_b{}^{x-1} = (\exp \Delta S_c/R)\,(\exp (x - 1)(T\Delta S_b - \Delta H_b)/RT) \quad (7)$$

Because this is valid for all x and j, the fundamental equilibrium constant K_b must be independent of what the functionalities are attached to, so K_b is related to the equilibrium concentration $Nf(1 - \alpha)$ of free functionalities and $Nf\alpha$ of reacted functionalities, th

$$K_b = \alpha/(1 - \alpha)^2\,Nf \quad (8)$$

From the last four equations:

$$w_x = \sum_j w_{xj} = w_1{}^x x\{\alpha/(1-\alpha)^2 f\}^{x-1} |G_M|^x \sum_j |G_{xj}|^{-1} \qquad (9)$$

The notion of a rooted tree is well known not only in graph theory (Harary[14]) but in its applications to chemistry since the work of Cayley in the nineteenth century. The notion occurs implicitly in previous methods of proving distribution (1) and in the attempt of Masson *et al.* to prove distribution (2). A molecule of the jth isomer of the x-mer fraction is turned into a graph by allowing the repeat units to form the nodes and the free functionalities to form the terminal points. Such a tree can then be rooted on any of its nodes and the branches ordered on the page to produce altogether T_{xj}, say, distinct node-rooted ordered forms, a process illustrated by Gordon and Temple[13]. From their theorem 2, which was established in a few lines, we obtain the special case

$$T_x \equiv \sum_j T_{xj} = x(f!)^x \sum_j |G_{xj}|^{-1}/f^{x-1} \qquad (10)$$

The order of the automorphism group $|G_M|$ of the graph-like (floppy) monomer is $f!$, that is, the number of permutations of the f functionalities. Accordingly,

$$T_x = x|G_M|^x \sum_j |G_{xj}|^{-1}/f^{x-1} \qquad (11)$$

and distribution (9) may be written

$$w_x = T_x w_1{}^x \alpha^{x-1}(1-\alpha)^{-2x+2} \qquad (12)$$

The number T_x of distinct node-rooted ordered x-mer trees is evaluated as a standard exercise in graph theory (compare Good[15]) without recourse to probability theory; T_x is the coefficient $C(\theta^x)\{\theta N(\theta)\}$ of θ^x in the generating function

$$\theta N(\theta) = \theta(1+u)^f \qquad (13)$$

with

$$u = \theta(1+u)^{f-1} \qquad (14)$$

By Lagrange's expansion[4]

$$T_x = C(\theta^{x-1})\{N(u(\theta))\} = (x-1)^{-1} C\{(u^{x-2})\}\{N'(u)(1+u)^{(f-1)(x-1)}\}$$
$$= f(fx-x)!/(fx-2x+2)!(x-1)! \qquad (15)$$

so that distribution (12) becomes

$$w_x = [f(fx-x)!/(fx-2x+2)!(x-1)!)] w_1{}^x \alpha^{x-1}(1-\alpha)^{-2x+2} \qquad (16)$$

It follows from the normalization condition for w_x that $w_1 = (1-\alpha)^f$ and this completes the proof of distribution (1) from standard statistical mechanics. Graph theory has merely served to evaluate the symmetry numbers occurring in partition functions.

Flory's account of gelation, now thirty years old, is sound, in spite of the attacks it suffers periodically. The state of matter near the gel point is of great importance not only to technology, but in biology[16,17] as will be further illustrated in a forthcoming article (R. C. Hider and M. G., to be published).

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Reply to Gordon and Judd

ALTHOUGH expressions similar to that of Flory[1] have been derived by several authors for the size distribution in branched polymers it has been assumed, implicitly or explicitly, in such derivations that the conversion α equals the probability that a functional group chosen at random has reacted. We have shown that, because functional groups never occur singly after their mutual condensation, but always in pairs, the choice between a "reacted" and an unreacted functional group is not meaningful. Our choice must lie between unreacted groups and reacted pairs. Flory's incorrect use of α in this respect led immediately to a divergence at $\alpha = 1/(f-1)$ in his expression for the size distribution. This led Flory, and subsequently many other investigators, to the belief that this divergence corresponded to the gel point. It is hardly surprising that others with the same assumption derived the same result as Flory.

Gordon and Judd do not directly contest our explicit criticisms of Flory's method, but rather claim to have derived the Flory distribution by another method. Their method is based on the use of a "fundamental" equilibrium constant, independent of chemical combinatorics, to describe the driving force of a chemical reaction[3]. The combinatorial entropy change is calculated separately from the symmetry numbers in rotational partition functions, with the aid of graph theory. In equation (8) of their paper, however, Gordon and Judd express this fundamental equilibrium constant K_b in terms of the experimental quantity α. This procedure is incorrect because α, of necessity, already includes all combinatorial effects.

In our method of deriving the distributions it is assumed that each molecule possesses an unreacted functional group. Our procedure automatically excludes from consideration the case of $f = 1$. That our treatment does not yield an acceptable result for this case is a measure of its consistency. We can, of course, readily modify our procedure to give the correct result for this case also.

The model common to all these treatments prohibits intramolecular condensation and therefore the point $\alpha = 2/f$ becomes a point of mathematical divergence. No characteristic of the model, however, requires a point of divergence at $\alpha = 1/(f-1)$, yet the normalization condition of Gordon and Judd can only be achieved in the range $0 < \alpha < 1/(f-1)$. A similar difficulty was encountered by Flory[4] who attempted to rationalize the result by claiming that it applied to only a part of the polymeric system under consideration (that is, to the "sol fraction"). In this respect, Flory altered his model to accommodate the result. No such difficulty is encountered with our expression, which applies over the entire range of α which the model allows.

It is now clear that Flory's theory of gelation cannot be correct. Evaluation of size distributions in branched polymers is important in silicate chemistry. Experimental evidence[5] confirms that Flory's theory is inapplicable to such systems.

We thank Professor Gordon for sending us a copy of his manuscript before publication.

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BIOLOGICAL SCIENCES

Induction of Growth in Newt and Frog Limbs after Perfusion with Extracts from Newt Blastemas

IT has been suggested that the nerves required for regeneration of the amphibian limb produce a "trophic material"[1,2]. Lentz[3] has suggested a "hormonal" role for the nervous system, but otherwise the nature of trophic material is undefined[4].

From our experiments with lower organisms[5–10], we found that the control of growth and differentiation is mediated through neurosecretion. For example, in *Hydra* small 25–35 Å particles, liberated by the nerve when large neurosecretory granules break down, participate in the control of growth and differentiation. Lentz[3] has shown particles of identical size in nerves of regenerating newts after limb amputation. We propose that in regenerating amphibians, the neurosecretory granule breaks down and is then most concentrated in those dividing cells which continually provide new binding sites for it, namely the blastemal cells.

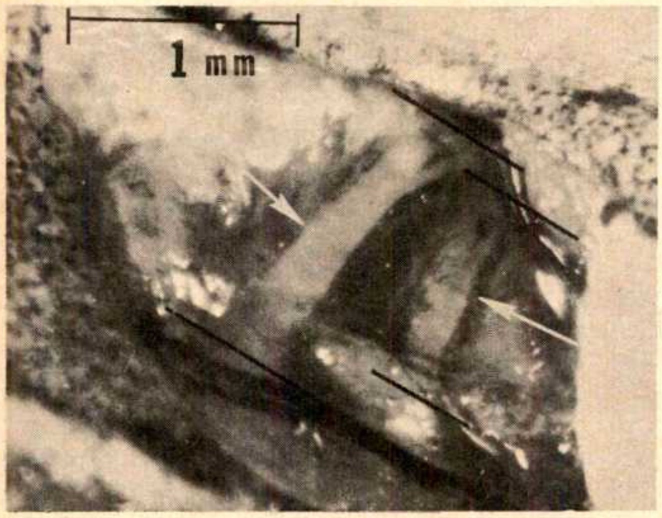

Fig. 1 A photograph of the brachial plexus (arrows) showing the two major nerves which constitute the plexus. A smaller third nerve of the plexus is not shown in the photograph. Lines show region of plexus removed by surgery (× 30).

We have investigated this possibility using the newt *Triturus viridiscens* (Lemburger, Wisconsin) and the frog *Rana pipiens* (Turtox Corporation, Chicago). Newts were kept at room temperature (25° C) in filtered aquaria and fed beef liver weekly. Frogs were kept in aquaria provided with a dry limestone shelf and fed twice weekly with *Tenebrio* larvae. The perfusion machine used was a Compact Infusion Pump, Model 975 (Harvard Apparatus Co., Inc., Massachusetts). Syringes (1 cm^3 plastic disposable) were attached to 1/2 inch needles with 27 bore hole.

Newts from which blastemas were obtained were excised through the mid-humerus. Developmental stages of blastema formation were examined by making a pin prick and squeezing blastemal cells into a drop of Ringer solution and examining them under Nomarsky illumination or phase microscopy at × 1,000. We found the number of mesenchymatous cells, which bind the 25–35 Å particle, to be greatest during a 20–30 day growth period following excision and we therefore used blastemas at this stage.

Blastemas were removed by cutting just distal to the initial excision site, and placed in a test tube surrounded by ice. Cold saline (4° C) was added to keep them moist during excision. The blastemas were micro-homogenized and then centrifuged in the cold (4° C) at 15,000 r.p.m. for 30 min. The supernatant was collected, diluted with 4.5 ml. of cold Ringer solution, and pipetted into aliquots of 0.3 ml. which were quick frozen in absolute alcohol/dry ice baths. An average of 392 blastemas was used for each preparation of extract. The frogs were excised mid-way along the humerus and treated as shown in Table 1.

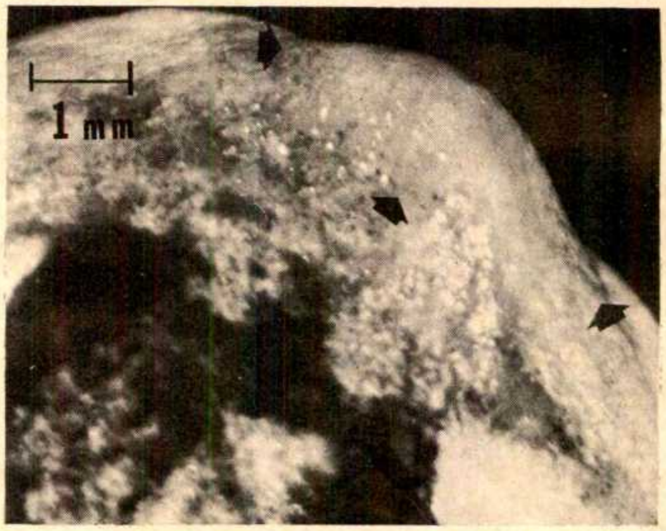

Fig. 2 The emergence of a blastemal tip on an animal which was injected in the centre of the excised arm. Note the arrows which show the extent of growth (× 12.75).

Perfusion of the frogs was begun 3 days after excision and continued every other day thereafter.

Denervation in the newts was accomplished not by simply excising the brachial plexus, but by complete removal of the nerve fibres (Fig. 1). Animals were denervated and sutured a day before the humerus was excised mid-way along its length. Naturally, it was important to reopen the animals periodically and determine if any nervous connexions had been established in the regions where the plexus had been removed. We found only one nerve connexion had been re-established and this particular animal was far behind in growth when compared with perfused animals.

Newts and frogs were tranquillized in a solution of tricaine methanesulphonate (MS222). Newts were perfused every other day with 0.05 ml. of extract over a 90 min period.

Six frogs were simply amputated along the humerus and used as control animals. They were not perfused. In these animals the wounds healed within 1 week, with piled up connective tissue at the wound site; no growth ensued. Frogs injected with collagenase alone (2 mg/ml.) or with Ringer solution behaved in the same way. Frogs injected with blastemal extract showed minimal growth but did not form a blastema. Those injected with blastemal extract plus collagenase (2 mg/ml.) did not heal but began to show pronounced blastemas (Figs. 2 and 3). In Fig. 3 the blastema indicated by an arrow is about to emerge from the tip of the wound. In Fig. 4 (both photographed 30 days after amputation) a much more pronounced blastema is forming, but its area is limited. During the formation of this blastema, it was pricked with a pin and thousands of cells were squeezed out onto a drop of Ringer solution on a slide. Examination with Nomarsky and phase microscopy showed these cells to be identical to mesenchymatous cells found in the newt's blastema. These pictures were taken more than 1 month before this writing and the blastemas are still growing.

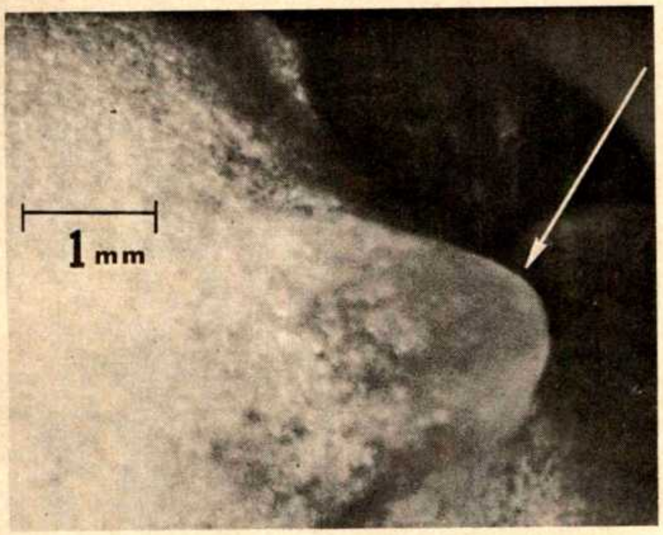

Fig. 3 A pronounced blastema in the frog which had been perfused basally with extract. Note the pronounced growth at the injection site. This tip of growth was found to contain a solid mass of mesenchymatous cells. The growth has continued for the past month and all indications are that a small limb will be regenerated (× 17.25).

If the needle is inserted directly through the centre of the wound, blastemal growth is general but smaller in length (Fig. 2). If the needle is inserted towards the edge of the wound, blastemal growth is regionalized and pronounced (Fig. 3).

Table 1 Treatment of Frogs

Animal	Type of perfusant	Amount (ml.)	Period of perfusion (min)
	Group 1		
1	Ringer solution	0.1	90
2	Collagenase (0.2 mg) dissolved in Ringer solution	0.1	90
3	Collagenase (0.2 mg) dissolved in extract	0.1	90
4	Extract	0.1	90
	Group 2		
5	Ringer solution	0.1	90
6	Collagenase (0.2 mg) dissolved in Ringer solution	0.1	90
7	Collagenase (0.2 mg) dissolved in extract	0.1	90
8	Extract	0.1	90

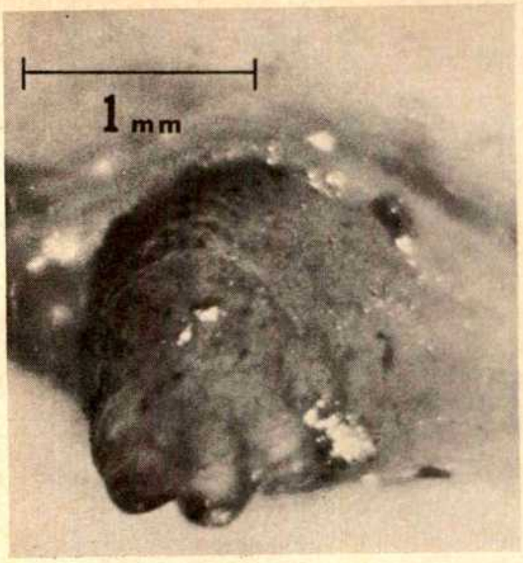

Fig. 4 The regrowth of a newt limb where nerve connexions were excised at the level of the brachial plexus. Since this photograph was taken, the animal has continued to form fully differentiated digits. In this photograph only the finger stubs are shown (× 30).

In newts, for three animals used in each trial, perfusion with Ringer solution not only inhibits growth but can cause the arm to deteriorate back to the shoulder girdle. Animals perfused every other day with a concentrated extract will be stimulated to maintain normal regeneration. In Fig. 4 the animal was photographed just as the digits were emerging at 2 months. It is important to note, however, that a well defined blastema was formed after the first 5 days of perfusion on all the animals receiving the extract. Control animals whose nerves have been excised and not perfused are exactly as those described by Deck and Futch[4]. In the beginning it seems that some blastemal growth is taking place, but this reaction soon ceases. The thickened epidermis and bulbous tip at the excised tip remain unchanged for 50 days.

We believe that the active material or inducer is a product of breakdown of a neurosecretory granule (demonstrated in newts by Lentz, but present in the same size and form in nerves of virtually every phylum examined with the electron microscope). We postulate that this compound is probably a small polypeptide in the same family as that found in coelenterates and flatworms. Our experiments will be repeated with perfusate separated by column separation followed by HVE paper separation; we hope that the substance which will promote normal growth in the absence of nerve in amphibia will also be applicable to higher animals.

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Cell-free Transmission of Mouse Neuroblastoma

AFTER the description of the cell-free transmission of neuroblastoma C1300, a transplantable tumour in strain A/J mice, by Prasad *et al.*[1], we made ten attempts to reproduce their results, first using their extraction procedure and then by using the viral concentration procedure of Moloney[2], modified by Huebner *et al.*[3]. We inoculated twenty-eight prenatal, forty-seven newborn, and sixteen 4-week-old A/J mice but failed to obtain positive results, even after 100 days postinoculation. Because we used newborn mice that are usually more susceptible to oncogenic viruses than the older mice used by Prasad *et al.*, and viral concentrates rather than filtrates, we expected to increase our chances of transmission.

We have found numerous intracisternal A-type particles and rare budding C-type particles in C1300 tumours, confirming the results of Prasad *et al.* In addition, we have found specific antigens of C-type RNA tumour viruses by the complement fixation test. A/J mice, like many other inbred and outbred strains of mice, are known to carry wild-type infectious C-type RNA viruses in spontaneous and transplanted non-leukaemic tumours, but except for the FBJ virus, no C-type RNA virus from solid tumours of any mouse strain has been shown to induce solid tumours of the original type.

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Effects of Amphetamine on Single Cell Activity in a Catecholamine Nucleus, the Locus Coeruleus

THE action of amphetamine on the central nervous system has been related to its ability to release and inhibit the re-uptake of dopamine (DA) and noradrenaline (NA) at presynaptic terminals[1-4]. Abundant catecholamine (CA) stores have been demonstrated in the cells of the locus coeruleus[5-7]. These two observations suggest that amphetamine causes the release and decreased re-uptake of CA from locus coeruleus cells. The drug, by promoting the accumulation of CA postsynaptically, might thereby initiate neuronal feedback inhibition of locus coeruleus units; such a mechanism has been postulated to explain biochemical observations on CA systems treated with amphetamine[8]. The opposite effect, feedback stimulation, has also been postulated to explain observations of the CA blocking effects of neuroleptics (chlorpromazine and haloperidol)[9-11].

To evaluate these hypotheses, extracellular microelectrode recordings were made from single neurones in the rat locus coeruleus, before and after treatment with amphetamine. Chlorpromazine was also given to evaluate its anti-amphetamine effects; such effects have been described previously in both clinical[12] and behavioural settings[13-15].

We used male Charles River rats weighing 225-300 g. Recordings were made by techniques similar to those previously described[16]. Animals were anaesthetized with chloral hydrate (400 mg/kg, intraperitoneally) and mounted in a stereotaxic apparatus. Coordinates, representing the outer dimensions of the locus coeruleus, were estimated by direct measurement from serial pontine sections of the brain from a Charles River rat, sectioned along the axes of König and Klippel[17]. A 3 mm burr hole was made at coordinates within the range of lateral 1,000-1,300 μm and posterior 1,700-2,200 μm. Tungsten microelectrodes with tip diameters of 1 μm were lowered through the burr hole by a hydraulic microdrive. Signals were passed through a high input-impedence amplifier and displayed on an oscilloscope. Unit rates were measured by an electronic counter whose analogue output was traced graphically by a potentiometric recorder. Signals from the oscilloscope (700-2,000 Hz) also drove an audio monitor.

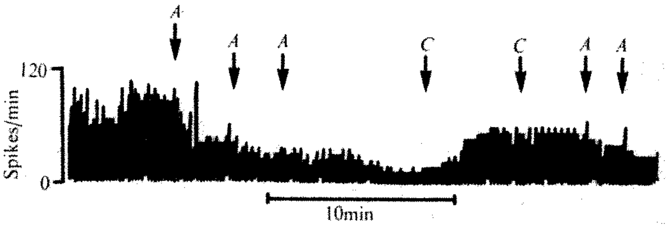

Fig. 1 Typical response of a locus coeruleus unit to amphetamine (*A*) and chlorpromazine (*C*). Spontaneous rate was 90 spikes/min. The record consists of the number of spikes counted over consecutive 10 s intervals. Within 30 s after the intravenous injection of amphetamine (0.2 mg/kg), a marked decrease in rate was observed. Two subsequent doses of amphetamine (0.4, 1.0) produced additional slowing (to 12 spikes/min). A recovery of rate to two thirds of the original was observed within 1 min after i.v. injection of chlorpromazine (1.0 mg/kg). Additional chlorpromazine (1.0) had no additional effect. Subsequent doses of amphetamine (0.5, 1.0) were less effective in decreasing the rate than in the untreated animal.

Only cells with a stable rate and a uniform spike amplitude were used. The waveform was observed for 5-10 min. Drugs were then administered intravenously to the tail in 0.05-0.2 ml. volumes given slowly over a period of 5-10 s. *d*-Amphetamine sulphate and chlorpromazine hydrochloride were given dissolved in distilled water at concentrations of 0.25 mg/ml. or 2.5 mg/ml. Only one unit was studied in each rat to avoid possible residual drug effects. At the completion of an experiment, the location of the electrode was marked by making an anodal electrolytic lesion (5 μA for 60 s). Animals were perfused through the left ventricle of the heart with a solution of 5% glutaraldehyde in saline. Serial frozen sections were cut at 50 μm and stained with cresyl violet. The location of each recording electrode was precisely identified in this manner. Fluorescent histochemical studies of the brain were carried out using the techniques described before[5,18-20].

Recordings were made from single units in thirty-five rats; subsequent histological examination showed that ten of these were in the locus coeruleus, and in these spontaneous activity decreased to less than one third of the original rate after small intravenous doses of *d*-amphetamine (Fig. 1). A marked response to amphetamine occurred with doses as small as 0.2 mg/kg. Larger doses produced further depression, the maximum depression of firing being achieved with 0.5-1.5 mg/kg (Fig. 1). Although in each recording a single prominent unit spike was monitored, multiple "background" spikes from neighbouring locus coeruleus cells also showed a gross reduction in frequency with amphetamine.

The twenty-five units recorded from regions outside the locus coeruleus were situated in the ventral lateral midbrain, central grey, pontine and mesencephalic reticular formations, and the ventral folia of the cerebellum. In fourteen (56%) of these, the rate more than doubled; in another four (16%) the rate decreased to one half to one third of the original with amphetamine doses from 0.25–3.7 mg/kg; and in seven (28%) there was no significant change in rate. In no case did a non-locus coeruleus cell show a reduction in firing rate to less than one third the spontaneous rate. Thus, the dramatic slowing response seen in locus coeruleus units after amphetamine treatment was unique among the units studied.

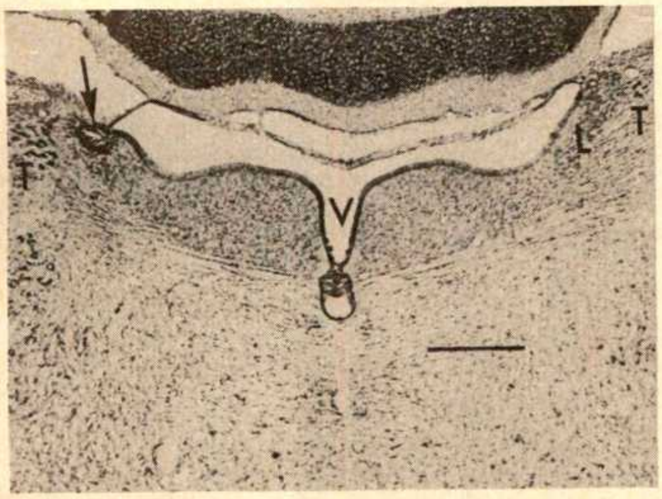

Fig. 2 Transverse histological section showing an electrolytic lesion (5 μA, 60 s) made through a recording electrode in the locus coeruleus on the left (arrow); a normal locus is seen on the right (L). V, Fourth ventricle; T, mesencephalic nucleus of the trigeminal nerve. Cresyl violet staining; scale, 0.5 mm.

Chlorpromazine (0.2–1.5 mg/kg) was given after amphetamine pretreatment in seven of the ten recordings from locus coeruleus units. In four of these there was a prompt return to nearly normal activity 1–2 min after intravenous chlorpromazine treatment (0.2–1.0 mg/kg). In these four units the effects of chlorpromazine were found to be partially reversible by additional amphetamine treatment, but the response to amphetamine was attenuated after chlorpromazine had been given and the depression of firing rate was only transient (Fig. 1). In the remaining three units pretreated with amphetamine there were only small or transient increases in activity after chlorpromazine treatment (0.8–1.5 mg/kg).

Neurones of the locus coeruleus differed from surrounding cells in their responses both to pharmacological stimulation and to somatic stimulation. In rats anaesthetized with chloral hydrate, locus units were found to have a slow rate of 1 to 2.5 spikes/s with a regular rhythm. In the immediate vicinity of the locus (within 500 μm), three additional cell types were often observed, one of which responded to touch. Some of these cells were sensitive to deep pressure and showed a two to three-fold increase in spontaneous rate post-stimulus; others were sensitive to light touch and showed transient bursts of discharges immediately after a stimulus. The second cell type was found to discharge in synchrony with respiration. In several of these cells there were bursts of 8–10 spikes before each inspiratory movement. Cells of the third type had firing rates which increased and decreased in very regular cyclic patterns (1–0.3 cycles per min). These cycles were not influenced by tactile, aural or visual stimuli but were markedly disrupted by small doses of amphetamine (0.05–0.5 mg/kg). These three cell types were different to locus coeruleus units, which were not synchronized with respiration and which rarely responded to tactile stimuli (two units showed transient post-stimulus suppression after deep pressure applied to the hind toes).

Cresyl violet-stained sections were used to identify the location of every cell from which a recording was made. This identification depended on microscopic examination of anodal lesions through the recording electrodes (Fig. 2). Our fluorescent histochemical results are consistent with the descriptions by Dahlström and Fuxe of their group A6 cells[5]. The histological appearance of group A6 is identical to the appearance of the locus coeruleus in routine cresyl violet stained sections (Figs. 2 and 3).

Our results show that amphetamine in small doses (0.2–0.5 mg/kg) produces a large decrease in the spontaneous rate of firing in units of a catecholamine nucleus, the locus coeruleus. A dose of 0.2 mg/kg decreases spontaneous activity to one half to one quarter of the original rate. Additional amphetamine usually produces additional depression of activity with a maximum effect being achieved at levels of 0.5–1.5 mg/kg. Although a small percentage of cells not in the locus coeruleus showed a decrease in spontaneous activity with doses between 0.5 and 2.0 mg/kg, the decrease never exceeded two thirds of the original activity. In contrast, locus units could always be depressed beyond this level with similar doses. Most cells outside the locus showed either an increase in rate or no change at all after amphetamine treatment (0.05–3.5 mg/kg). Excitatory effects of amphetamine administered parenterally in other regions of the brain[21,22], including some serotonin-containing cells of the midbrain raphe nuclei[23], have been described already.

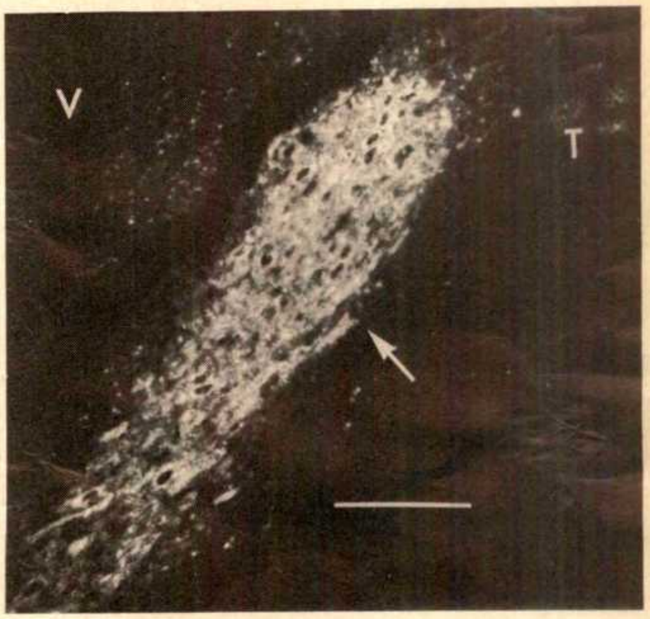

Fig. 3 Fluorescence micrograph of locus coeruleus (arrow) in normal rat brain. The locus parallels the floor of the fourth ventricle (V). Three faintly autofluorescent cells of the mesencephalic nucleus of the trigeminal nerve (T) are seen adjoining the nucleus along its dorsal lateral border; scale, 0.1 mm.

The responses to chlorpromazine were less uniform than those to amphetamine. In four out of seven locus coeruleus cells in which chlorpromazine (0.2–0.4 mg/kg) was given, a prompt and nearly complete reversal of amphetamine effect was observed. Additional increases in rate were not observed with total doses exceeding 1.9 mg/kg. These responses to chlorpromazine were transiently and only partially reversible with further doses of amphetamine. The remaining three cells showed only small or transient increases in rates after chlorpromazine (0.5–2.0 mg/kg) treatment. It is not yet clear why there was a variable response to chlorpromazine. Nor is it known what effect chlorpromazine has on spontaneous activity of locus cells in the absence of amphetamine.

The mechanism by which amphetamine reduces the rate of firing in cells of the locus coeruleus might be related to a direct action on the locus cells or to an action at some other central or peripheral site. On the basis of biochemical observations, it has been proposed that, in the central nervous system, amphetamine releases presynaptically bound NE or DA and blocks their re-uptake[1–4,24,25]. Amphetamine treatment would be expected to promote the pre-synaptic release and post-synaptic accumulation of catecholamines at locus coeruleus terminals. Our results are consistent with the suggestion that by promoting the pre-synaptic release of catecholamines with amphetamine, a feedback inhibition of CA neurones can be produced[8].

Several other hypotheses concerning the action of amphetamine should also be considered. It might function as a sympathomimetic amine[26,27], acting directly in the central nervous system. If it does, the results from this experiment would suggest that reduction of the rate in locus cells is caused by either a direct inhibitory response to sympathetic input or an indirect feedback inhibition from a post-synaptic neuronal circuit. Pretreatment with α-methyl tyrosine, an inhibitor of CA synthesis, may be of use in distinguishing between these direct and indirect sympathomimetic actions. Another mode of amphetamine action might be related to an induced alteration of neuronal input to the locus coeruleus. One type of altered input might be secondary to peripheral adrenergic effects of amphetamine, but this hypothesis seems unlikely in that peripheral adrenergic effects are negligible after small doses of amphetamine (0.2–1.0 mg/kg)[23]. Finally, some unique action of amphetamine on locus coeruleus cells is a possibility which has not been ruled out.

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Influence of Histoincompatibility between Mother and Foetus on Placental Size in Mice

ALTHOUGH the mammalian foetus is a natural allograft because it inherits paternal strain antigens histoincompatible with the mother, frank manifestations of rejection do not occur. (Explanations for this phenomenon have already been reviewed[1–7].)

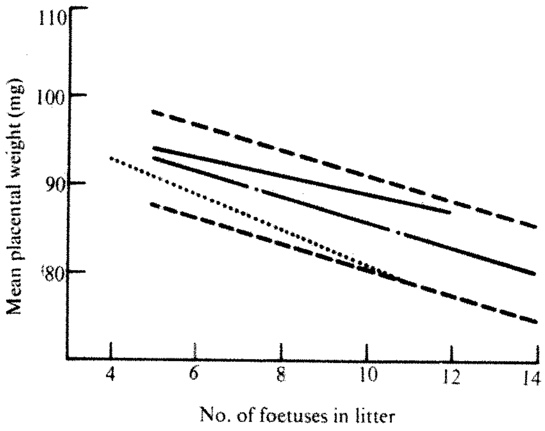

Fig. 1 Least squares regression lines of mean placental weights on numbers of foetuses in isogeneic (– · –), congenic (. . . .) and allogeneic (—) crosses (groups I, II and III respectively). Equations of least squares regression lines, and standard error of estimate, for each group are as follows: Group I: $y = 100.47 - 1.45x \pm 5.30$; group II: $y = 101.01 - 1.99x \pm 4.72$; group III: $y = 98.95 - 1.02x \pm 3.91$. Standard error for the isogeneic group is indicated graphically (- - -).

Placental size in mice tends to increase when mother and foetus are histoincompatible[8]. When two inbred strains, C57BL ($H\text{-}2^b$) and A2G ($H\text{-}2^a$), were crossed, placentae of F_1 foetuses were significantly larger than those from corresponding isogeneic crosses. Transplantation of homozygous blastocysts from one strain into the uteri of pseudopregnant females of the allogeneic strain showed that this difference is attributable to antigenic dissimilarity rather than heterozygosity[8]. This effect was also observed in crosses of C57BL females and C3H ($H\text{-}2^k$) males[9]. Furthermore, C57BL mothers immunized against paternal A2G antigens produced hybrid progeny with larger placentae than those of corresponding hybrid progeny from non-immunized mothers[10,11]. Moreover, mothers rendered tolerant at birth to paternal strain antigens produced placentae smaller than those from untreated mothers bred to allogeneic males, and virtually equivalent in size to those from control inbred litters. Crosses of *Peromyscus maniculatus*, the deermouse, and *P. polionotus*, the oldfield mouse, however, showed that placental weights of foetuses from reciprocal hybrid crosses differed significantly from each other as well as from the parental types, and that the mean placental weight for one of the hybrid combinations was significantly smaller than that of the corresponding inbred mating[12].

In an attempt to correlate quantitatively the amount of placental enlargement with the degree of histoincompatibility between parental strains of mice, young adult virgin females of the C57BL/10Sn (H-2^b) strain were divided into three groups and mated at approximately 90 days of age to isogeneic males, males of the congenic B10.A (H-2^a) strain, and males of the allogeneic A/J (H-2^a) strain, groups I, II, and III, respectively. Females were killed 17.5 days after the appearance of the vaginal plug. The uterus was removed and placed on filter paper moistened with normal saline. Foetoplacental units were removed from the uterus and then foetus, foetal membranes and umbilical cord were cut away from each placenta. Placentae were then gently blotted between two saline-moistened filter paper disks and weighed to the nearest milligram on a spiral spring balance. No significant difference was found between mean placental weights of litters with zero and one reabsorbing foetus, so both litter categories were included in the statistical analysis. Litters containing two or more reabsorbing foetuses were not included in the statistical analysis. Litters are considered in terms of the number of live foetuses rather than the total number of implantations, after McLaren[9]. Breeding was continued until data for twenty litters of each of the three crosses were accumulated. The mean placental weight for each litter was plotted according to the number of foetuses in the litter. Regression lines were fitted to these data by the method of least squares. The relation of mean placental weight to the number of foetuses in the litter for the three crosses is shown in Fig. 1.

Table 1 Foetal Survival and Histocompatibility

Group	Mother	Foetus	No. of litters	No. of implantations	Mean No. of implantations per litter and s.d.	Survival (%) of implanted conceptuses to day 17.5 of gestation
I	C57BL	C57BL × C57BL	30	241	8.03 ± 2.98	87.6 (211/241)
II	C57BL	C57BL × B10.A	31	259	8.35 ± 2.20	86.1 (223/259)
III	C57BL	C57BL × A/J	29	251	8.66 ± 2.14	91.2 (229/251)

Litters from the three crosses show a negative regression of mean placental weight on increasing litter size. There is no significant difference in the positions of the three regression lines nor are their slopes significantly different.

Thus, in this study, the H-2^b × H-2^a cross produced no significant increase in placental size relative to the corresponding isogeneic cross, whereas in previous experiments such increases were observed[8,10,11]. Although the paternal strains, A/J and A2G respectively, are immunogenetically identical at the major H-2 histocompatibility locus, they are certainly not identical at all minor histocompatibility loci. Indeed, if the phenomenon of placental enlargement were attributable to histoincompatibility at these minor loci, then the difference in results between this study and previous ones might be explained by such a mechanism, rather than by invoking differences in experimental techniques or statistical methods.

There was a tendency to an increased number of implantations per litter with increasing histoincompatibility between mother and foetus. There was also an increased percentage survival of implanted conceptuses to day 17.5 of gestation for progeny of the allogeneic cross compared with those of the isogeneic cross. But neither of the tendencies is statistically significant (Table 1).

Studies in the rat have shown that excess heterozygosity for **Ag-B** histocompatibility antigens among backcross progeny is due to increased homozygote susceptibility to postnatal wasting disease resembling a classic graft-versus-host reaction[13,14]. It was suggested that histoincompatibility at minor transplantation loci is responsible for this decreased postnatal survival and that superimposition of histoincompatibility at the major Ag-B locus reduces this selective disadvantage, perhaps by a mechanism involving immunological enhancement and steric hindrance[14].

Thus, in spite of the lack of statistical significance of the data in Table 1, there are indications that heterozygosity and consequent histoincompatibility with the mother at the major H-2 transplantation locus may confer on the foetus a selective prenatal survival advantage. If the mechanism proposed here operates in a similar fashion during gestation in mice, then the similarity of the percentage survival values for the progenies of the isogeneic and allogeneic crosses may be due to compensation in the latter by superimposition of H-2 incompatibility on non-H-2 incompatibilities and hence enhancement of survival to the isogeneic histocompatible level.

The design of this study did not permit investigation of possible deleterious effects of minor locus histoincompatibility in the absence of superimposed H-2 incompatibility. Experiments are now in progress to evaluate this proposed effect and the combined effects of major and minor locus histoincompatibilities on both prenatal and postnatal viability of heterozygous progeny.

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Relationship between Antibody-mediated Immunosuppression and Tolerance Induction

ANTIBODY-MEDIATED immunosuppression is no longer thought to be solely due to the masking of antigen by antibody. The hypothesis that events beyond the binding of antibody to antigen are operative in antibody-mediated immunosuppression is supported by the following facts. (1) Antigen-masking need not be complete to obtain pronounced suppression of immune responses[1,2]; (2) interactions between antigenic determinants on the same immunogenic particle (molecules to whole cells) take place so that suppression of immune responses to one antigenic determinant may occur with the binding of antibody to another non-cross-reacting and topographically separate antigenic determinant[3-5]; (3) parts of the antibody molecule, other than that involved in the binding of antigen, are important in the regulation of the immune response by antibody[6-9]; (4) immunosuppression does not necessarily become more pronounced when the dose of passively administered antibody is increased but proceeds through an optimum beyond which less suppression is observed[10,11,13,14]; and (5) immunosuppression by antibody can lead to inactivation of the antigen-sensitive cell population[12-14]. Similarly, immunological tolerance is no longer thought to be the simple elimination of immunologically competent cells by antigen. The following data suggest a more complex mechanism in the induction of immunological tolerance. (1) Animals which demonstrate tolerance seem to possess both sensitized lymphoid cells and soluble factors (antibodies or antigens) which prevent the sensitized cells from functioning[15,16]; (2) induction of tolerance is often preceded by the production of measurable antibody[31] or antibody-forming cells[17,18]; (3) induction of tolerance requires the presence of a functioning complement system[19]; and (4) cells capable of binding antigen remain, or may increase, during the attainment of the tolerant state[20-23]. Consequently, it now seems possible that these two hyporeactive states, antibody mediated immunosuppression and immunological tolerance, share common characteristics and common modes of induction.

Teams in two laboratories have demonstrated the optimal effect with regard to immunosuppression by antibody[10,11,13,14]. In both cases, optimal immunosuppression was achieved by certain doses of antibody; if more antibody was added, the degree of immunosuppression became less. In Diener and Feldmann's experiments[13,14], the optimal effect was demonstrated in terms of the degree of inactivation of immunocompetent cells, whereas we assessed the degree of suppression of the 19S antibody-forming cell response[10,11] and of 7S immunological "memory" on cell transfer[10]. In both experimental systems[10,11,13,14], the quantity of antibody which gave the optimal suppression was likely to be less than that needed for complete covering of all antigenic determinants. In these experiments, the suppressive antibody was administered passively, but data are available to suggest that endogenously produced antibody is capable of inducing feedback regulation of immune responses[24].

Fig. 1 indicates the relationships which have been reported to exist between dose of antigen and either (1) the concentration of antigen in tissues or (2) the amount of antibody which is formed in the initial immune response. The concentration of antigen in tissue bears a simple linear relationship to the amount of antigen which is administered[25,26]. On the other hand, the amount of antibody formed initially does not follow a simple straight line antigen dose–response relationship, but a sigmoidal or plateau response characteristic of many biological responses[28-31]. Because of the straight line relationship for antigen in tissues and the sigmoidal relationship for initial mmune response, four phases or zones should be discernible s one proceeds from low to high doses of antigen. There is a hreshold dose of antigen below which no initial immune reponse is induced. This is followed by a zone where the production of antibody is minimal and insufficient to react with all the tissue antigen. As the dose of antigen is increased further there is a rapid increase in the amount of antibody formed initially so that antibody excess is attained. With even greater doses of antigen, the amount of antigen in tissues will be in excess even if the initial antibody response remains maximal. Therefore, there is a low and high zone of antigen doses where antigen in tissues would be in excess of the antibody produced initially, while there is an intermediate zone where the concentration of antibody would be in excess of the amount of antigen in tissues. From experiments indicating that certain low levels of passively administered antibody which do not saturate antigen suppress immune responses maximally[10,11,13,14], one could deduce that the zones of tissue antigen excess over antibody produced would lead to suppression of immune responses (tolerance), whereas the zone of antibody excess would allow continuation of immune responses. Such a relationship between immunological responsiveness and dose of antigen has been reported by Mitchison[31].

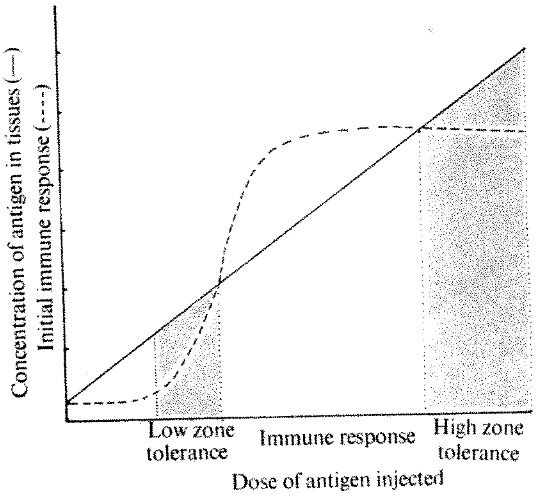

Fig. 1 Relationship between dose of antigen and either concentration of antigen in tissues (———) or level of initial antibody response (- - -). Zones where antibody is present but not in excess of antigen in tissues represent tolerizing conditions ("low and high zone tolerance"), whereas the zone where antibody is present and in excess of antigen in tissues allows a continuance of the immunologically responsive state ("immune response"). A dose of antigen which leads to the presence of tissue antigen but no induction of the immune response does not alter the immune capacity.

In summary, we propose that immunological tolerance develops when an immune response is regulated by the presence of antigen–antibody complexes in relative antigen excess. This theory accounts for the following observations: (1) low and high zone tolerance with an intermediate zone of heightened immunological responsiveness, (2) antibody or general immunoglobulin formation in the early phases of tolerance induction, (3) the role of complement indicating the presence of complement-fixing antigen–antibody complexes in the induction of tolerance, (4) antibody and immunologically competent cells present at some time in classically tolerant animals (the antibody and cells may disappear in long standing tolerance), and (5) evidence which suggests that normally reactive cells become inactivated when injected into tolerant animals.

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Thymus–Marrow Cell Interaction evaluated by PHA Stimulation and Graft versus Host Activity

THERE is now abundant evidence for cooperation in certain immune responses between B and T lymphocytes[1] which are respectively of bone marrow and thymus derivation. B cells have been shown to secrete antibody but the helper role of the T cell is less well defined. It has also been suggested that in mice PHA responsiveness can be an exclusive characteristic of T cells[2]. Experiments will be presented in this paper which can be interpreted to indicate that the capacity of dissociated thymus cells to respond to phytohaemagglutinin (PHA) *in vitro* can be much augmented by the presence of bone marrow cells which could be thought to have a helper role in this respect. A small series of experiments is also presented which suggests that a similar form of cooperation can take place in graft versus host responses.

The basic design of experiment involved culture of newborn mouse thymocytes and adult mouse bone marrow in the presence of PHA. In the parallel series of experiments the same kinds of parental cells were injected singly or in combination into F_1 hybrid recipients in order to induce a graft versus host reaction.

CBA, C57BL and (CBA × C57BL)F_1 hybrid mice of both sexes were used as thymus and bone marrow donors. Bone marrow cells obtained from femurs and tibiae of normal 4-6 month old animals were diluted to 2×10^6 viable cells/ml. in Hanks–Eagle minimal essential medium (MEM), containing 20% foetal calf serum (FCS, Gibco). Intact thymus lobes from newborn (2–7 days) and adult (4–10 months) animals, cleaned to avoid mediastinal lymph node contamination, were gently pressed through a multilayer nylon sieve and cell concentration was fixed at 2×10^6 viable cells/ml. in MEM. Triplicate cultures with and without 0.025 ml. PHA (Wellcome), containing $2\text{–}6 \times 10^6$ cells in a standard volume of 3 ml. MEM, were prepared from thymus and bone marrow cell suspensions (group *A*). Mixtures of both in varying ratios were also set up (4 : 1 to 1 : 4) (group *B*). Another group of cell mixtures (group *C*) was prepared according to a modified technique for one-way directional cultures by using mitomycin C (30 μg/ml., A. Christiaens s.a., Brussels) treatment to inhibit DNA synthesis of one of the two cell populations in culture[3]. Cultures were kept for 24–96 h in a 5% CO_2 atmosphere at 37° C. DNA synthesis was determined in all the groups by adding 1.5 μCi/ml. ^{3}H-thymidine (^{3}H-TdR) 6 h before harvesting and measuring the radioactivity in a liquid scintillation spectrometer[3,4].

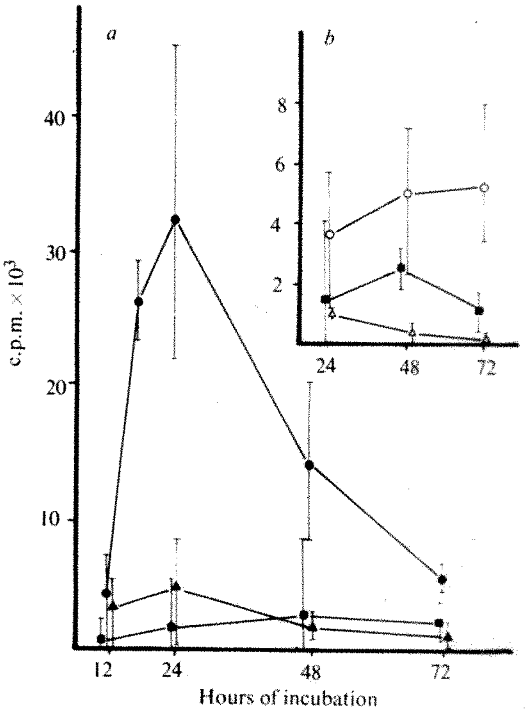

Fig. 1 ^{3}H-TdR incorporation induced by PHA in thymus–marrow cell mixtures. Values refer to 4×10^6 thymocytes and 2×10^6 unfractionated marrow cells/culture (c.p.m. × 10^3): difference in incorporation between PHA-stimulated cultures and the respective unstimulated controls (PHA-C). ■, Bone marrow; ▲, newborn thymus; △, adult thymus; ●, newborn thymus + bone marrow; ○, adult thymus + bone marrow.

In parallel with these *in vitro* assays, differing amounts of CBA thymocytes, bone marrow or both, mixed in different proportions, were injected into F_1 hybrid litters in order to evaluate possible increments in graft versus host activity of the mixtures (group *D*). Spleen index was calculated on day 9 and values above 1.30 were considered positive.

When newborn thymus cells were mixed in various proportions with syngeneic bone marrow, a remarkable increase of thymidine uptake in PHA stimulated cultures was observed. This response depended on the number of thymocytes in the mixture and the optimal thymus marrow concentration was $4 + 2 \times 10^6$ cells/culture; peak response was usually detected at 24 h (Fig. 1*a*). But when adult thymocytes were mixed similarly with marrow cells, a slight increase in ^{3}H-TdR uptake was observed, which was not statistically significant (Fig. 1*b*).

Data obtained from one-way directional cultures show that the PHA response of unblocked cell mixtures and mitomycin-blocked marrow cells in culture with intact thymocytes is strikingly similar. Highest response was achieved in both mixtures when a 2 : 1 thymocyte : marrow ratio was employed within the limit of 4×10^6 thymus cells/culture (Fig. 2). Beyond this limit a significant response was still registered, albeit reduced. No significant increase in PHA response was seen when blocked thymocytes were cultured with intact marrow cells. Moreover, an increase in the number of blocked marrow cells over 2×10^6 cells/culture did not further enhance the response of a fixed number of unblocked thymocytes.

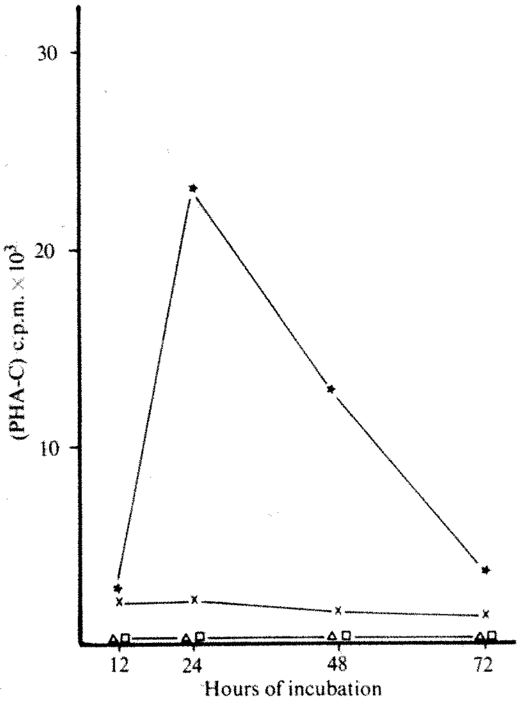

Fig. 2 ^{3}H-TdR incorporation induced by PHA in thymus-marrow, one-way directional cultures. △, (NT) (newborn thymus); □, (BM) (bone marrow); ★, NT+(BM); ×, (NT)+BM; ○, mitomycin-treated.

Finally, Table 1 summarizes some of the results obtained by the Simonsen assay, by injecting thymus and marrow cell suspensions mixed in various proportions or administered as single cell suspensions. It is evident that bone marrow cells are devoid of graft versus host activity at the doses employed, while immunocompetent cells of this type are detectable in newborn thymus cell suspensions. In most cases, however, the respective thymus–marrow cell mixtures showed an increase well above the expected sum of the spleen indices obtained by injecting the same cell suspensions separately. No graft versus host activity was expressed by adult thymocytes injected separately or in mixture with marrow cells.

No fully satisfactory explanation can be offered for our findings. It seems that cells from the thymus of newborn mice can respond to PHA but only to any significant degree in the presence of syngeneic bone marrow cells. Previous experiments[5,6] have indicated that a glass adherent cell population derived from bone marrow is less effective in enhancing the response of newborn thymocytes which suggests that the effect observed is not macrophage-mediated. The response observed by newborn thymocytes in contact with adult bone marrow plus PHA was different in that the peak of tritiated thymidine incorporation occurred at 24 h rather than at 48 h which is characteristic of mouse peripheral blood lymphocyte populations in our system. It could be argued that a newborn mouse thymus contains more "mature" cells about to emerge into the periphery where they would form part of the PHA-responsive lymphocyte pools than does an adult mouse thymus. The helper role of the bone marrow has to be elucidated further and is difficult to relate to T and B cell cooperation theories. It is still uncertain whether bone marrow and thymus contain the mature form of either cell species. Thus, in a further series of experiments we shall seek similar synergism between T and B cells derived from secondary rather than primary lymphoid organs.

Table 1 Immunocompetence of Thymus and Bone Marrow Cell Mixtures

Cell type	Cell dose (× 10⁶)	Spleen index* Mean	Range	Positive tests/total	%
Bone marrow	10	1.06	(1.01–1.15)	0/8	0
	20	1.06	(0.77–1.17)	0/8	0
	30	1.03	(0.99–1.12)	0/4	0
Newborn thymus	10	1.14	(0.97–1.49)	1/4	25
	15	1.30	(1.02–1.83)	3/9	33
	20	1.52	(1.06–2.00)	13/18	72
Bone marrow and newborn thymus	10+10	1.61	(1.23–2.25)	8/10	80
	10+15	1.55	(1.28–1.87)	13/15	87
	10+20	1.81	(1.44–2.12)	8/8	100

* Calculated according to Simonsen[6] at day 9. Results refer to 108 animals injected with cells and fifty-four controls injected with medium. Values over 1.30 were considered positive.

The close similarity between the results of PHA stimulation and graft versus host assay by thymus–marrow combinations is intriguing but faces many of the interpretative problems already alluded to. It hints, however, at the possibility that certain kinds of PHA responsiveness can be used as a measure of the capacity to engender the sort of cell-mediated immune responses which are involved in graft versus host reactions.

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Multiplication of the Scrapie Agent

ALTHOUGH the transmission of scrapie by the inoculation of filtrates of tissue from affected animals suggests that the agent multiplies in the cells of the host, there is little published evidence of its propagation in cell cultures. Gustafson and

Kanitz[1] reported that cell cultures could be established more readily from scrapie-affected sheep or mice than from normal animals and that material from the twenty-third pass of one such cell line was infective for mice. Only two of seven mice reacted, however, so the titre was apparently low and it was not clear whether there had been actual multiplication of the agent or whether this activity was derived from the original tissue.

At Compton we have established a cell line[2,3] from the brain of a mouse which was showing clinical signs following intracerebral inoculation of the strain of the scrapie agent adapted to mice by Chandler[4]. This line has now been taken through 100 serial passes. To determine whether the agent was multiplying in these cells or merely persisting from the original brain tissue a sample of every fifth passage was titrated intracerebrally in mice. The activity was found to be $10^{2.2}$ ID_{50}/0.05 ml. by the fifth pass and to vary between $10^{1.1}$ and $10^{3.5}$ up to the hundredth.

At the twenty-fifth and again at the sixty-fourth passage level, titrations were made of the level of activity in the cultures at various times after seeding. From the results it seemed that the increase in activity was proportional to the cell count and that this reached a peak at about the time the monolayers were complete. Thereafter the activity seemed to remain constant at least up to 35 days.

No differences were demonstrable when titrations were made in such a way that the cells were kept as intact as possible or when the cells were fragmented by trituration and freezing before the serial dilutions were prepared. It thus seemed that there might be only one active site in each affected cell.

Although the titres which were obtained were comparatively low, the activity in cultures was apparently confined to the cells or cell fragments and the agent was not being released from the cells into the fluid. The proportion of cells to fluid in cultures is of course far lower than that in brain, so that, if the activity is related to cell content, the relative value may not actually be greatly different from that in brain. In cell cultures the scrapie agent seems to multiply in synchrony with and as an integral part of the cells and could be likened to such entities as prophage, plasmids or the transforming factor of an inactivated virus such as SV40, rather than to complete virions which multiply independently. It differs from these entities in its remarkable resistance to various physical and chemical treatments. If the scrapie agent multiplies only in relation to the cells, this could account for the slow, progressive nature of the disease.

Which cells are involved in the multiplication of the transmissible agent of scrapie? Eklund, Kennedy and Hadlow[5] were impressed by the early development of agent in organs such as the spleen and lymph nodes and suggested that cells of the lymphocytic series might be involved, which might explain the apparent lack of antibody response. But antibody response to antigens such as sheep red cells is apparently unimpaired in scrapie-affected animals[6] and no morphological changes in the lymphocytes have been observed. Gustafson and Kanitz[1] suggested that astrocytes were the cells observed in their cultures; but although the astrocytes are hypertrophied in scrapie they do not appear to increase in number.

We believe the "target cells" in scrapie may be reticulo-endothelial in origin. Reticulo-endothelial cells are represented in the central nervous system by microglia, which increase in number in scrapie. Although it is not possible to identify the cells in our infected cultures, they resemble morphologically the cells described by Gustafson and Kanitz as astrocytes. When the cells in our cultures were injected intracerebrally into mice, colonies developed in which the histological appearance of the cells suggested that they were mesodermal in origin and more likely to have been derived from microglia than from astrocytes. Support for the belief that cells of the reticulo-endothelial system are concerned in the scrapie reaction is the finding of Haig and Pattison[7] that capillary cells are active in organ cultures of scrapie brain and that of Buening[8] that the cells cultured from scrapie mouse brains were apparently oligodendroglia, microglia and capillary pericytes.

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Taurine—a Possible Neurotransmitter?

Apart from the dicarboxylic acids, taurine is the most abundant amino-acid in the nervous system[1], and yet very little is known about its function[2]. It has been suggested that taurine acts as a transmitter; Curtis and Watkins[3] have evidence that among other amino-acids, taurine when applied iontophoretically to the vicinity of a neurone in the central nervous system exerts an inhibitory effect on the rate of firing and, furthermore, there is a structural resemblance between γ-aminobutyric acid (GABA) and taurine. There are also similarities in the distribution of both these amino-acids and in the localization of their synthesizing enzymes in different regions of the brain[4]. In addition, after density gradient centrifugation of rat brain homogenate, both cysteinesulphinate decarboxylase activity and taurine has been found to be enriched in the nerve ending fractions[4]. Glutamate and cysteinesulphinate decarboxylases are closely similar enzymes[5] and their activities increase in parallel during development of rat brain[4].

In extending this work we have examined other criteria supporting the view that taurine is a transmitter substance. Since GABA and other transmitters are released on stimulation we have first studied the release of taurine on applying

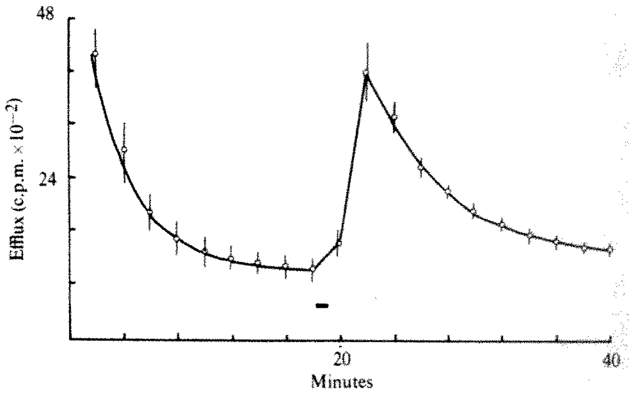

Fig. 1 Release of taurine from stimulated rat cortical slices. Slices preloaded with ^{35}S taurine were incubated in oxygenated Krebs–Ringer medium. ^{35}S-released into the medium is plotted (○) together with the s.e.m. for five estimations. The preparation was electrically stimulated for 1 min (solid bar) and samples of the medium collected every 2 min for estimations of radioactivity.

electrical pulses to tissue slices perfused with Krebs–Ringer medium as described by Srinivasan, Neal and Mitchell[6]. Slices (120 mg) prepared from the cortex of young adult rats (about 150–200 g body weight) were pre-incubated with 1.6×10^{-5} M ^{35}S-taurine for 15 min in 20 ml. of oxygenated Krebs–Ringer medium together with amino-oxyacetic acid (10^{-5} M). (The latter compound inhibits the metabolism of GABA and was included to keep conditions identical to those of the GABA experiments, although it has no known effect on taurine metabolism.) After 30 min the slices were collected by rapid filtration and transferred to a perfusion cell through which taurine-free oxygenated Krebs–Ringer medium was pumped. Samples were collected for radioactivity determination before and after stimulation by rectangular pulses of 60 Hz (duration 2 ms; current 1 mA; voltage 40–80 V). Fig. 1 shows that there is a rapid efflux of ^{35}S from the tissue comparable with that found in similar conditions for GABA[6]. To show the release of ^{35}S to be taurine, brain slices and medium, after and before stimulation, were extracted with 10% (w/v) trichloroacetic acid and washed four times with ether. Extracts were separated on ascending paper chromatography in butanol : acetic acid : water (12 : 3 : 5 by volume) and by high voltage electrophoresis in formic-acetic acid buffer, *p*H 1.86, at 7 kV. In all cases a single peak of radioactivity coincided with that of a standard sample of taurine.

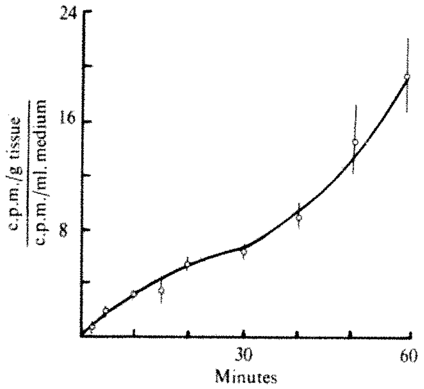

Fig. 2 Uptake of ^{35}S-taurine into rat cortical slices. Brain slices (10 mg wet weight of cortex) were incubated in 10 ml. of oxygenated Krebs-phosphate medium at 37° C. After 15 min ^{35}S-taurine was added to the medium to a final concentration of 5×10^{-7} M. Slices were collected by filtration and rinsed before determining radioactivity at various times of incubation with taurine. Estimations (○) are recorded together with s.e.m. for at least four determinations at each point.

If taurine is released on stimulation, as our experiments suggest, an efficient process for the termination of its action should be available. Since the enzymatic conversion of taurine to isethionic acid in rat brain is too slow to fulfil this role[7] we have looked for a transport system that could efficiently remove taurine from the extracellular fluid of the brain. In preliminary experiments uptake of very low concentrations of ^{35}S-taurine into slices of rat brain cortex has been found with no detectable metabolism of taurine. Fig. 2 shows the uptake of taurine at 5×10^{-7} M into brain slices; the curve has been fitted to the mean result at each concentration. Further work will be necessary to establish the detailed kinetics of the process and the exact form of the uptake curve. These experiments indicate that uptake is a possible mechanism for the inactivation of taurine and the provisional calculated K_a supports the view. The K_a (apparent K_m) for this uptake process was estimated by measuring the uptake of taurine between concentrations of 2.5×10^{-6} M and 10^{-3} M in the medium into brain slices. The amount of radioactivity in the tissue after 10 min of incubation was used to calculate the rate of uptake and a value of $K_a = 5 \times 10^{-5}$ M was obtained (compared with GABA where $K_a = 2.2 \times 10^{-5}$ M). Such a process has also been considered likely to apply at synapses where GABA is thought to be released[8].

It would be premature to conclude that taurine is a transmitter or modulator in the nervous system, for much work on specific antagonists and its localization within identifiable neurones is still essential. Our work does indicate an interesting similarity in release and uptake mechanisms between GABA and taurine, and there are sufficient resemblances in localization and biosynthesis of the two amino-acids to warrant further study.

We thank Dr J. F. Mitchell and Mr C. Rayner for their help in the release experiments. L. K. K. holds an MRC studentship.

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DDT in California Sea Lions

WE wish to report extraordinary concentrations of DDT residues* in California sea lions, *Zalophus californianus*, which inhabit year round the coastal waters of California and Baja California, Mexico[1]. These waters receive agricultural runoff from California valleys where DDT has been used extensively[2–4], and where residues have been increasing in the primary stages of some coastal pelagic food chains[5].

Tissue samples of blubber, and in some cases, brain liver and muscle, were collected from animals of both sexes and various ages between September 19 and December 10, 1970. These were four apparently healthy adults (one male and three females) shot at San Miguel Island, 56 km from Santa Barbara, and one adult male killed near Año Nuevo Island, 31 km north of Santa Cruz, California, six dying males stranded on beaches between Santa Cruz and San Francisco which were killed in the laboratory, and fourteen fresh male carcasses found on or near Año Nuevo Island. Tissue samples weighed approximately 50 g, were frozen immediately after collection, and stored at −68° C until chromatography was performed according to the methods of Stanley and LeFavoure[6] and Kadoum[7].

DDT residues, while present in all samples, predominated in blubber (Table 1). The breakdown of total DDT residues was similar for all animals in both blubber and brain (Table 2). An analysis of DDT residues according to sex and age revealed no significant differences.

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* DDT residues refer to all the constituents of commercial DDT and its metabolites: *p, p'*-DDT (1, 1, 1-trichloro-2, 2-*bis*(*p*-chlorophenyl) ethane), *p, p'*-DDD (1, 1-dichloro-2, 2-*bis* (*p*-chorophenyl) ethane), and *p, p'*-DDE (1, 1-dichloro-2, 2-*bis* (*p*-chlorophenyl) ethylene).

Table 1 DDT Residues in Healthy, Sick, and Dead California Sea Lions: Means and Standard Deviations, Number of Specimens in Each Group (Parentheses) and Ranges

Group	Total DDT residues			
	p.p.m. wet weight		p.p.m. lipid weight	
	Blubber	Brain	Blubber	Brain
Healthy—killed	906 ± 640	8.6 ± 5.8	1,220 ± 860	85 ± 53
	(5)	(4)	(5)	(4)
	41 to 1,929	0.2 to 16	47 to 2,436	3.1 to 146
Sick—killed	689 ± 164	13 ± 2	1,022 ± 336	140 ± 29
	(6)	(5)	(6)	(5)
	400 to 903	8.9 to 16	552 to 1,387	98 to 190
Fresh carcasses	1,006 ± 645	14 ± 11	1,687 ± 1,280	173 ± 147
	(14)	(6)	(14)	(6)
	258 to 2,678	2.6 to 34	333 to 5,077	23 to 431
Totals: all specimens	911 ± 582	12 ± 8	1,452 ± 1,104	138 ± 105
	(25)	(15)	(25)	(15)
	41 to 2,678	0.2 to 34	47 to 5,077	3.1 to 431

To investigate whether some of the high concentrations in carcasses were due to tissue decomposition after death, blubber and brain samples were collected from a sick animal immediately after death, 2 days later, and once again 5 days after death. During these 5 days, the carcass was left outdoors and covered with burlap sacks. Total DDT lipid values in serial order were 1,267, 1,167 and 1,268 p.p.m. for blubber and 146, 147 and 147 p.p.m. for brain. Evidently, concentrations in these tissues did not fluctuate significantly during this time period.

Table 2 Percentage of DDT and its Metabolites in Blubber and Brain: Means and Standard Deviations

	p.p.m. lipid weight	
	Blubber (N = 26)	Brain (N = 15)
DDE	93.9 ± 1.9	94.1 ± 3.4
DDD	3.9 ± 1.3	3.3 ± 1.1
DDT	2.2 ± 1.1	2.6 ± 1.2

DDT residues in the muscle of four healthy adults averaged 1.2 ± 0.8 p.p.m. wet weight and 418 ± 246 p.p.m. lipid weight. Mean concentrations in the liver of four healthy adults and three subadults which had been killed in the laboratory, combined, were 17 ± 10 p.p.m. wet weight and 677 ± 229 p.p.m. lipid weight.

The DDT residues in the blubber and brains of these sea lions are higher than those reported in other marine mammals[8-13]. Maximal values equal those in brown pelicans, *Pelecanus occidentalis*[14-18]. We do not know the effects of high DDT concentrations on California sea lions, but studies on other animals suggest several possibilities—reproductive failure[19-21], decreased resistance to stressful infectious agents[22,23], and an acute toxic effect on the central nervous system[24].

Abortions in California sea lions have increased since 1968 on several rookeries off the coast of California and Baja California, Mexico[21]. A systematic census on San Nicolas Island yielded a count of 135 aborted foetuses in 1969 and 442 in 1970, more than a three-fold increase from one year to the next[25]. We counted 283 one-week-old pups at Islas San Benito and Isla San Martín, Mexico, between May 25 and May 28, 1971—133, or 47%, of them were dead.

Between August 25 and November 30, 1970, Mrs J. Schonewald of the California Academy of Sciences received 420 reports of sick or dead sea lions observed between Monterey and Fort Bragg, California. An epidemic was publicized nationally (for example, *San Francisco Chronicle*, October 14, 1970, and *New York Times*, October 15, 1970) with death being attributed to the bacterium, *Leptospirae*, which was isolated in some of the animals.

It is doubtful that the increased mortality resulted from an acute toxic effect of DDT since concentrations in carcasses were not significantly higher than in the living animals. Second, concentrations of DDD and DDT, combined, in the brains of carcasses are far below the lower limit of 30 p.p.m. suggested as the direct cause of death in birds[24].

The potential danger of organochlorine pesticides to pinnipeds warrants our concern, for it involves not only these marine mammals but man, whose diet often includes fish and cephalopods.

We thank J. Carr, R. Gantt and R. C. Hubbard for collecting samples; J. Phillips and D. Murphy for chromatography; D. M. Robinson for transportation, and R. Hinegardner for helpful suggestions. This study was supported in part by a grant from the National Science Foundation.

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Light Flashes produced in the Human Eye by Extremely Relativistic Muons

IT is generally agreed that the light flashes observed by astronauts on Apollo missions 11–14[1] were produced by the passage of heavy cosmic ray nuclei through the eye. The exact mechanism has been a subject of some controversy, however, most workers leaning towards either Čerenkov radiation[2–4] or direct ionization and excitation of molecules at the retina[1,5,6]. Light flashes similar to the Apollo observations have been reported to result from irradiations of the eyes by X-rays[5,7], neutrons[5,6,9,10] and slow alpha particles[8], all of which are more likely to involve ionization and excitation than Čerenkov radiation. Early indications that the human eye might be sensitive to individual relativistic singly charged particles[11] have not been borne out by calculations[3] or by recent observations[5].

This report describes a test of the ability of the human eye to detect Čerenkov radiation when it is generated with sufficient intensity by the passage of a burst of relativistic charged particles through the vitreous humour and retina of the eye. The small values of LET and total dose involved in producing the bright extended flashes described below seem to rule out any significant contribution from direct ionization and excitation. All observations were made during two short periods of exposure to a beam of 6 ± 2 GeV/c muons at the Brookhaven AGS. Red X-ray dark adapting goggles were worn for at least 0.5 h before exposure and observations were made in a completely darkened state under improvised cloth and leather hoods with the muons entering the eye through the side of the head. The muons arrived spread over pulses of 440 ms duration with a time interval of 2 s between pulses. The flux density of muons in each pulse was approximately 3×10^3 muons cm^{-2}.

The phenomena appeared as bright diffused flashes which appeared and disappeared with the beam pulses and seemed to fill the periphery of the field of view but never the entire field of view. When I turned away from the beam so that it entered from the rear of the head, the flashes were no longer clearly distinguishable. The coincidences between announced flashes and the beam pulses were checked as well as my ability to tell when my eyes were centred in the active beam.

Localized areas of the retina function as units at threshold levels of signal. The areas of these summation units range from 10^{-6} cm^2 at the fovea to about 9×10^{-4} cm^2 on the periphery with an average of roughly 8×10^{-5} cm^2. Signals generated in a unit within an interval of 0.1 s are effectively in coincidence. The number of such coincidences required to induce a visual sensation is somewhere between two and twenty, ten being typical of most measurements[12].

There is some possibility that the flashes observed in this experiment are similar in origin to the haze reported in X-ray[5,7] and neutron[6] irradiations of the eye, phenomena that would certainly not involve Čerenkov radiation. But the flux rate that resulted in bright extended flashes corresponds to the passage of three muons per pulse through a 9×10^{-4} cm^2 summation unit on the periphery or less than 1 in each 0.1 s interval of beam. This rate of dose, 0.026 mr in 0.1 s, is a factor of ten smaller than the X-ray doses over the same or shorter intervals that were required for even a slight haze[5,7] despite the similarly low LET associated with both radiations. Moreover, the 10 s persistence reported for the neutron produced haze[6] was not observed in this experiment.

On the other hand, the number of "visible"[3] Čerenkov photons in each 0.1 s of pulse that can be expected to accompany the muons through the retinal summation units has been calculated[13] as 40 on the periphery, 0.1 at the fovea and about 4 for a unit of average area. If we assume the probability of absorbing each photon incident on the periphery to be 20%, the value measured at 10°–20° eccentricity[14,15], then a threshold value of ten absorbed photons should be exceeded in the muon experiment for 26% of the peripheral units in each 0.1 s interval of the 0.44 s pulse and essentially nowhere else on the retina. Although calculations of this type are necessarily crude as a result of our incomplete knowledge of the peripheral region of the retina, they do indicate Čerenkov radiation as the most plausible mechanism for producing the flashes described above.

I thank members of the Columbia, Harvard, National Accelerator Laboratory, and Rochester University collaboration who designed and operated the muon facility at the Brookhaven AGS for help, Professor L. Lederman for helpful suggestions and Dr Paul Bottino for help with the observations.

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BOOK REVIEWS

Vertebrate Past

Vertebrate Palaeozoology. By Everett C. Olson. Pp. xiii + 839. (Wiley Interscience: New York and London, May 1971.) £14.25.

It is rare—and highly refreshing—to find a textbook in any subject which makes a completely new approach. This Professor Olson has achieved. The conventional textbook tells the reader what is known; where difficulties arise they are glossed over or sometimes ignored altogether. The intention is to produce a self-contained synthesis which gives the student a clear and intellectually satisfying picture of the basic structure—and the excellence of the textbook varies inversely with the number of inconvenient facts omitted.

Vertebrate Palaeozoology has a different aim and follows a different pattern. The author sets out to give an overall picture of the present state of the science, to relate the animal to its environment and to clothe the hard parts in living flesh. But a much more significant and valuable innovation is that we are spared none of the difficulties, rather are they carefully spelled out for us. Thus the man who is teaching in any branch of vertebrate palaeontology can get an up to date picture of the state of knowledge in that field, and, what is perhaps more important, the certainty of that knowledge. The research worker can see how work is progressing in fields related to his own, and can perhaps find it valuable in suggesting research problems for his graduate students. Most valuable of all, however, the student can really see what science—as exemplified by vertebrate palaeontology—is all about—how it consists at any time of a mass of facts: some connected reasonably firmly by theory, some strung together by tentative and rather unsatisfactory hypotheses and some just sticking out like sore thumbs and refusing to fit in comfortably anywhere. As pedagogic methods change and student studies increasingly range more widely and, as an inevitable concomitant, become shallower, the experience of being asked a question by a student, answering honestly "I do not know" and seeing the look of outraged horror on his face, will become commoner. Professor Olson's book is a useful corrective to students falling into the error that either their teachers or their textbooks embrace, in their own field, the whole of knowledge.

The book is divided into four sections. The first deals with the history of the Vertebrata in broad outline and in a rather summary manner—it is short (52 pages). The second section is entitled "Vertebrate Morphology and Function"; it is larger (114 pages); and its scope is adequately illustrated by its title. The third section is considerably longer than either of the first two (262 pages) and is entitled "The Classification of the Vertebrates". This covers rather more than is suggested by the title of the section, and includes a considerable amount on the phylogenies of the taxa.

The last section is the longest of all (385 pages) and deals in detail with five special topics: the problems of life in water, the radiation of the Actinopterygii, the conquest of land, the origins of the Mammalia and the influence of palaeogeography on evolution. This section inevitably overlaps to some extent with the one that precedes it. The book is well illustrated but has no plates.

The only major criticism of the book is its price: £14.25 is ridiculous for such a book and ensures that its only purchasers will be libraries and the more affluent senior workers. This is a pity, as it would be invaluable for teaching graduate students and undergraduates taking advanced courses; and at a more realistic price it could well be prescribed as a class textbook. K. A. Kermack

Travels of Banks

Joseph Banks in Newfoundland and Labrador, 1766. His Diary, Manuscripts and Collections. By A. M. Lysaght. Pp. 512 + 103 plates. (Faber and Faber: London, August 1971.) £15.

The name of Joseph Banks is most familiar as the associate of James Cook on his epic voyage around the world in the Endeavour (1768–71), and since the bicentenary celebrations in Britain and Australia this connexion has been many times reinforced. Banks's part in that voyage has to some extent been misinterpreted by later commentators who have represented him as the gentleman amateur, a dilettante naturalist of wide interests but little application. In other eyes Banks was the organizing genius and employer of a well chosen band of scientists and illustrators whose contribution to natural history would have been profound had not sickness and death broken up his team on the return journey.

That Banks made a voyage to Newfoundland and Labrador in 1766 is little known, and in many ways this cruise on the Niger was a rehearsal for the later Endeavour voyage. There is no doubt that it furthered his interest and competence in natural history and set a standard of biological exploration which was to be maintained throughout his later voyages. In April 1766 Banks and Constantine John Phipps joined the Niger, a 32-gun frigate of 679 tons. They spent the months from May to October in the region between St John's, Newfoundland, and Labrador, collecting, exploring, and studying the local inhabitants, their life, economy, and particularly their operation of the great fisheries there. In these five months (four in fact as Banks was ill for most of July) he collected or recorded 340 species of plants, 91 species of birds, and a number of fishes and invertebrates. In addition he kept a journal of his general activities as well as more detailed botanical and zoological notebooks. This all amounted to a considerable achievement for a young man of 23 on his first expedition, especially in the cramped and rigorous conditions of a naval frigate of 1766.

Dr Averil Lysaght's book is a scholarly appreciation of Banks's work in this region of North America. She has printed his diary (now in the library of the Royal Geographical Society of Australia, South Australian Branch), the detailed descriptions of animals and a few plants (now in McGill University Library), and a catalogue of the names and localities of the plants (now in the British Museum (Natural History)). Strangely, Banks's journal is a very impersonal affair and the man remains something of an enigma. Nowhere does he allow his feelings to obtrude on the factual statements of the day's activities, and his stay in Lisbon at the end of the journey sounds to have been a dull and uneventful time which impression is, however, shown to be false by the relevant letters and notes. These major manuscripts are supplemented by lists of the animals preserved in spirits or of birds' skins, and other original observations, but the whole is welded together with such a wealth of explanatory notes and biographical detail that there is rarely a question comes to mind that is not already answered in a complete manner elsewhere in the book. Lysaght also sheds some interesting new light on Banks's previous acquaintance with Cook (for it has been claimed that they first met on the deck of the Endeavour just before she sailed in 1768). In fact it seems that Cook and Banks could well have met in St John's harbour in 1766, for Cook's surveying vessel Grenville arrived there at least a day before the Niger sailed, and it seems impossible that the Niger's passengers would not have seized the opportunity to meet the already respected navigator and cartographer.

The illustrations in the volume deserve special mention. Both the twelve colour plates, those of birds painted by Sydney Parkinson and Peter Paillou, and the plants by G. D. Ehret, and the 91 monochrome illustrations add greatly to the interest of the work. The quality of reproduction of the plates and the presentation of the whole book reflect great credit on the designer and publishers.

This masterpiece of historical scholarship will stand as a fitting memorial to Banks's work, and must be some reward to the author for many years of unstinting study of eighteenth century natural history. ALWYNE WHEELER

Effects of the Pill

Metabolic Effects of Gonadal Hormones and Contraceptive Steroids. By Hilton A. Salhanick, David M. Kipnis and Raymond L. Vande Wiele. (Based on a Workshop held in Boston, Massachusetts, December 1–5, 1968.) Pp. xxix + 762. (Plenum: New York and London, 1969.) $27.50.

WITH the introduction of oral contraceptives we have experienced the first, and still only major, application of mass medication to previously healthy and asymptomatic, but potentially diseased, individuals. It was inevitable that such extensive usage of the products of the pharmaceutical industry would bring in its wake a host of drug-induced and drug-exacerberated diseases and that this would in turn lead to intensive investigation into their prevalence and nature.

Sufficient evidence was available by 1968 to justify holding a conference devoted to the metabolic effects of gonadal hormones and contraceptive steroids, the proceedings of which became the subject of this review. Although most biochemical changes produced by the contraceptive steroids are not associated with overt disease the data collected together in this volume leave no room for doubt that as a group this class of compounds has profound metabolic effects on most, if not all, systems of the body. They do not, as was once supposed, act only on the endocrine and reproductive organs.

This book is composed of fifty-two chapters, each written in the form of an "original" article, which are grouped together into nine separate sections, each dealing with a different body system. The editors have wisely not followed the current fashion of including verbatim all of the discussion after each paper. Instead they have selected and pruned it. This enhances rather than detracts from the value of the book which is a commendable record of the experimental basis of knowledge of the metabolic and biochemical effects of the steroidal contraceptive agents up to and including 1968. VINCENT MARKS

Proteinase Action

Proceedings of the International Research Conference on Proteinase Inhibitors, Munich, November 1970. Edited by H. Fritz and H. Tschesche. Pp. ix + 304. (Walter de Gruyter: Berlin and New York, 1971.) 108 DM.

THIS volume contains the proceedings of the first international research conference on proteinase inhibitors which was held in Munich in November 1970.

The conference covered a wide area and started quite rightly with four contributions on proteinase inhibitors in human medicine. Following these contributions, which provide a basic orientation, there are three papers on specific isolation methods. Then both the theory and methods of studying the inhibition mechanism are outlined by six contributors. The conference then passed further afield and the book contains articles on inhibitors from plant tissues. The most well understood proteinase inhibitor, the basic bovine compound, is thoroughly chewed over by eight different authors. In this section I found much of the meat of the proceedings. Inhibitors from pancreas, seminal fluid and miscellaneous sources are also described. The subject is certainly comprehensively covered.

Heimburger's group from the Behringwerke, Marburg, describe the isolation of six different proteinase inhibitors from human serum, all of which contain some carbohydrate. Although an earlier hypothesis that α_2 macroglobulin had an insulin carrier function was not confirmed, it was observed at the conference that this α_2 macroglobulin is identical to the single protein of serum which can bind zinc. It has been reported to be high in diabetes.

The isolation methods described include water insoluble trypsin resins (Fritz *et al.*, who were the first to use affinity chromatography in this area), chymtrypsin-sepharose (Feinstein) and trypsin-sepharose (Kassell and Marciniszyn).

The molecular structures of some crystalline proteinases are outlined by Shotton who shows the common structural pattern and their specific binding sites. To this is added the very satisfying and elegant results of Huber and co-workers in Munich who have established the atomic structure of the basic trypsin inhibitor of bovine organs. This molecule has several very interesting structural features; it is dominated by a substantial amount of anti-parallel β-pleated sheet and also contains some polyproline II helix.

Many of the contributions show clearly that this subject is becoming extremely well defined as the techniques of protein chemistry are increasingly applied to the problem. This work will be of great value to everybody interested in proteinase action and its control. S. SHALL

Mass Spectrometry

Mass Spectrometry. Vol. 1. Senior Reporter D. H. Williams. Pp. ix + 323. (The Chemical Society: London, February 1971.) £7.

THIS is the first of a series of specialist volumes promised and it is appropriate to ask what its intended function might be. It seems to me to represent an extension of current Chemical Society publications, in fact to be a mixture of two of them. The first, sixth and seventh chapters are reminiscent of *Quarterly Reviews* and the remainder of *Annual Reports.* A clearer sense of purpose may emerge in later volumes.

The rapid expansion of mass spectrometry is well indicated by the contents of this book which is necessarily very comprehensive, not to say compressed. In particular there are chapters on alternative methods of ionization and analysis; computerized data acquisition and handling; gas chromatography–mass spectrometry; energetics, kinetics and ion structures; reactions of specific functional groups; natural products including oligosaccharides; and organometallic and coordination compounds. This last chapter clearly indicates the rapid rise in the popularity of metallocene chemistry for, notwithstanding the length of this section, there is barely occasion for more than a mention of all the results reported.

There are voluminous references and an adequate index. The chapters are all written by well known practitioners in the respective fields and are, in general, clearly written and readily understood. The book is well produced and although rather expensive is not excessively so for these days.

The spelling is sometimes unusual, for example colinear (page 23 legend Fig. 3) and there are some trivial errors (page 67, line 17 should read "mass spectrometer". Moreover, SI units are nowhere mentioned, the traditional Torr and kilocalories being preferred.

ROWLAND I. REED

CORRESPONDENCE

Synthetic Pyrethrins

SIR,—We would like, on behalf of the pyrethrum industry, to comment on the article "Pyrethrin Prospects" (*Nature*, **233**, 441; 1971).

We cannot agree with your viewpoint that the pyrethrum industry will suffer a "fate" similar to certain natural products. Incidentally, the one you mention, quinine, is said to be doing extremely well.

It may be worthwhile to look at some facts about synthetic pyrethroids. Initially, Allethrin, which got off the ground in America as a strategic contingency measure, declined at the end of the war and survived in Japan only under a heavy discriminatory tariff against imported natural pyrethrum. This tariff being still in existence, it comes as no surprise that the new generation of synthetics being manufactured there are enjoying similar protection. To put the new synthetic products in a nutshell, what you get, at least for aerosols, is either an economic level which results in good kill with medium knockdown, or an uneconomic level which gives good knockdown and overkill: hardly an easy choice for the formulator.

The point about lower acute toxicity rates (rat) for synthetics is interesting academically, though it does not summarily relegate natural pyrethrins into a separate toxicity class. At least one synthetic pyrethroid sank without trace during its development stage, because of high mammalian toxicity. We do not know if the toxicity figures for synthetic products represent chemically pure specimens or the practical commercial materials, but believe that the manufacturers ought to state what solvents, aromatic or otherwise, are used. Again, no assay method exists for determining synthetics in the presence of aromatic solvents, pyrethrins and synergists.

We are rather surprised that natural pyrethrins should be labelled as causing sneezing, when for years aerosol formulators have known[1] that one or two commercially produced synergists are more indictable. Indeed, lately one of the new synergists, 'Tropital', has appeared on the market claiming specifically "non-sneezing" properties. We cannot agree that the prices which you quote for synthetics make them competitive with pyrethrins. All pyrethroids are certainly out of the class of organochlorides, and always have been, but this is a point hardly at issue these days. The new technique of ultra-low volume dispersement (ULV), especially by aircraft, opens up a huge range of uses for pyrethrins hitherto closed, due to the adverse economics of the quantities involved. In addition, interesting new repellency factors are being established about pyrethrum, which also offer new uses.

Where the synthetics *have* succeeded has been due to recent shortfalls in the production of natural pyrethrum. This was caused in East Africa by a switch-over to high content pyrethrum clones, which coincided with unusual drought conditions and led to the loss of many plants and a severe overall setback in production. The rationale of producing high content pyrethrum plants, however, is that, with no more effort, two or three times the quantity of pyrethrum can be produced from the same weight of dried flowers, and the economics of this are obvious.

Yours faithfully,

D. R. MACIVER

Director

The Pyrethrum Bureau,
PO Box 420,
Nakuru, Kenya, East Africa

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[1] Zucker, A., "Investigation of Purified Pyrethrum Extracts", *Annals of Allergy*, **23** (1965) (vide *Pyrethrum Post*, **8** (3), 7–9).

Phosphate Detergents

SIR,—I think that the article by your Washington correspondent putting down the environmentalists ("Algae Better Than Burns", *Nature*, **233**, 229; 1971) was in itself somewhat hasty. The movement towards phasing out phosphates certainly did not occur overnight. And I find it hard to believe that the detergent manufacturers have really spent "millions of dollars" testing alternatives. I believe that he has simply quoted company rhetoric without verifying it, which is as reprehensible in an editorial as it would be in a scientific paper. After all, what is needed to perform a scientific test of a detergent's effectiveness but a washing machine and a few dirt-stained collars? This used to be proved nightly on television. The abuses to the environment (and thus to ourselves) can and will be stopped: the ecology movement is not going to go away. Once that is accepted, the priorities become clear. To have made a wrong move (if indeed it was) on the way to the right goal is not a tragedy. I think that the reason so many people have been jumping into ecology with both feet lately is that they have discovered the indescribable bliss that comes from ceasing to do something wrong.

Yours faithfully,

MARK WIRTH

10212 Capitol View Avenue,
Silver Spring, Maryland 20910

SIR,—In three recent issues of *Nature* (**233**, 229, 295, 362; 1971), you have discussed the dilemma over phosphates in detergents. But there is one question with which you have not concerned yourself: are phosphates necessary to get a wash clean? This, I believe, is a crucial question. Detergent manufacturers have claimed that everyone's wash will come out a tattletale-grey if we stop using detergents, whether these detergents contain phosphates or a phosphate-substitute. This is simply not true.

I tried an experiment where I put two extremely dirty laboratory coats in with my regular weekly laundry. I used only soap and washing soda. Both coats came out white. I will not deny that phosphates do help to get a wash clean, but I am convinced that a high percentage (40–60 per cent) is quite unnecessary. (Another point: high-phosphate washday products are invariably high priced.)

For these reasons I cannot go along with the Environmental Protection Agency's unreserved endorsement of phosphates. If they had endorsed low-phosphate (10–20 per cent) detergents only, I could understand that. But to say in effect that high-phosphate detergents are necessary for a clean wash, and that we have no choice but to put up with the pollution from them, is economic and ecologic nonsense.

Yours faithfully,

GRETCHEN LUEPKE

Office of Marine Geology,
US Geological Survey,
345 *Middlefield Road,*
Menlo Park, California 94025

Errata

In the article "Unique Bedrock and Soils associated with the Teesdale Flora" by G. A. L. Johnson, D. Robinson and M. Hornung (*Nature*, **232**, 453; 1971), an unfortunate transposition of lines occurred. The first three lines of column 2, page 454, should follow immediately after the fifth line of the section "Whin Sill and Metamorphism" in the first column of the same page.

In the article "Extended Sleep and Performance" by John M. Taub, Gordon G. Globus, Eric Phoebus and Robert Drury (*Nature*, **233**, 142; 1971), the first sentence of paragraph 4 should read: "Table 1 shows the average number of minutes spent in each sleep stage, wakefulness, and total sleep time during both nights of each sleep condition". It should be noted that Table 1 does not include total time in bed, and that reference 8 is not cited in the text.

In the article "Retraction and Expansion of the Dendritic Tree of Motor Neurones of Adult Rats induced *in vivo*" by B. E. H. Sumner and W. E. Watson (*Nature*, **233**, 273; 1971), the second sentence of paragraph 2 should read: "200 µm low viscosity nitrocellulose . . .".

Reports and Publications

not included in the monthly Books Supplement

Great Britain and Ireland

The Natural Rubber Producers' Research Association. Thirty-third Annual Report. Pp. 48. (London: The Natural Rubber Producers' Research Association, 1971.) [197

King Edward's Hospital Fund for London Annual Report for 1970. Pp. 39. (London: King Edward's Hospital Fund for London, 1971.) [197

Glasshouse Crops Research Institute. Annual Report for 1970. Pp. 210. (Rustington, Littlehampton: Glasshouse Crops Research Institute, 1971.) £1.25. [197

Advisory Committee on Gas Council Researches—Report 1969–70. Pp. 11. (Leeds: The University, 1971.) [197

Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 269, No. 1201 (15 July 1971): A Unified Theory of Conjugate Flows. By T. B. Benjamin. Pp. 587–647. £1.50; $3.90. Vol. 270, No. 1202 (16 July 1971): A Discussion on Solar Studies with Special Reference to Space Observations. Arranged by the National Committee on Space Research under the leadership of Sir Harrie Massey, C. W. Allen, A. H. Gabriel, B. E. J. Pagel and R. Wilson. Pp. 1–195 + plates 1–10. £5.90; $15.40. (London: The Royal Society, 1971.) [197

Proceedings of the First International Symposium on Biological Control of Weeds, March 1969. Edited by Dr. F. J. Simmonds. (Miscellaneous Publication No. 1 of the Commonwealth Institute of Biological Control, Trinidad.) Pp. vii + 110. (Farnham Royal, Slough: Commonwealth Agricultural Bureaux, 1970.) £2. [197

Department of Education and Science. Scientific Research in British Universities and Colleges, 1970–71. Vol. 1: Physical Sciences. Pp. xxiii + 841. £6.50 net. Vol. 2: Biological Sciences. Pp. xxiii + 706. £6 net. Vol. 3: Social Sciences (Including Government Departments and Other Institutions). Pp. xxxii + 608. £5.50 net. (London: HMSO, 1971.) [207

Africa, America, Asia, Europe, Oceania: Family Planning in Five Continents. Pp. 34. (London: International Planned Parenthood Federation, 1971.) [207

The Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom. A Compendium of University Entrance Requirements for First Degree Courses in the United Kingdom in 1972–73, excluding Degree Courses for External Students. Pp. 288. (London: The Association of Commonwealth Universities, 1971.) £1.30. [227

International Index of Laboratory Animals. Second edition. Pp. viii + 89. (Carshalton, Surrey: Medical Research Council, Laboratory Animals Centre, 1971.) £1. [227

The Scientific Proceedings of the Royal Dublin Society. Series A. Vol. 4, No. 1: The Stratigraphy and Structure of the Moinian and Dalradian Metasediments of the Mullet Peninsula, Co. Mayo, Ireland. By J. S. Sutton. Pp. 1–14. 50p. Vol. 4, No. 2: Some Conspicuous Participants in Palaeozoic Symbiosis. By C. H. Holland. Pp. 15–26 + plate 2. 50p. Vol. 4, No. 3: The Lower Carboniferous (Dinantian) Stratigraphy of the Carrigaline Area, Co. Cork, Ireland. By Michael E. R. Le Morvan. Pp. 27–36 + plate 3. 50p. Vol. 4, No. 4: A Collection of Irish Bank Vole Skulls. By J. S. Fairley. Pp. 37–44. 50p. Vol. 4, No. 5: Preliminary Palaeomagnetic Results from Some Irish Limestones of Carboniferous Age. By I. R. McAulay and P. Morris. Pp. 45–55. 40p. (Dublin: Royal Dublin Society, 1971.) [227

The Countryside Commission. Countryside Information Directory. (London: The Countryside Commission, 1971.) [227

Other Countries

Current Contents—Science and Technology, Vol. 1, No. 1, January 1971. Pp. 1–94. Published monthly. Subscription: Rs. 36; £4.15; $10. (Gurgaon, Haryana, India: Indian Documentation Service, 1971.) [137

Atlantide Report No. 11: Scientific Results of the Danish Expedition to the Coasts of Tropical West Africa, 1945–1946. Pp. 243. (Copenhagen: Danish Science Press, Ltd., 1970.) 90 Danish Kr. [137

US Department of the Interior: Geological Survey. Professional Paper 521–C: Geology of the Paleozoic Rocks, Navajo and Hopi Indian Reservations, Arizona, New Mexico and Utah. By J. H. Irwin, P. R. Stevens and M. E. Cooley. Pp. iii + 32 + 2 plates. Professional Paper 521–D: Hydrogeology of the Cenozoic Igneous Rocks, Navajo and Hopi Indian Reservations, Arizona, New Mexico and Utah. By J. P. Akers, J. C. Shorty and P. R. Stevens. Pp. v + 18 + 2 plates. Professional Paper 658–C: Mesozoic Stratigraphy of the Santa Rita Mountains, Southeast of Tucson, Arizona. By Harald Drewes. Pp. v + 81. $1.50. (Washington, DC: Government Printing Office, 1971.) [137

New Zealand Department of Scientific and Industrial Research: Geophysics Division. New Zealand Seismological Report—Inangahua Earthquakes 1968. By R. D. Adams, M. A. Lowry and D. E. Ware. Pp. 280 + 12 maps. (Wellington: Government Printer, 1971.) [157

Metropolitan Life. 1970 Report to Policyholders. Pp. 16. (New York: Metropolitan Life Insurance Company, 1971.) [157

Background Study for the Science Council of Canada. Special Study No. 15: Scientific Activities in Fisheries and Wildlife Resources. By D. H. Pimlott, C. J. Kerswill and J. R. Bider. Pp. 191. (Ottawa: Information Canada, 1971.) $3.50. [197

Australian Journal of Zoology, Supplementary Series. Supplement No. 4: The Tabanidae (Diptera) of Australia. V. Subfamily Tabaninae, Tribe Tabanini. By I. M. Mackerras. Pp. 54. (East Melbourne: CSIRO, 1971.) [197

CSIRO, Australia. Annual Report of the Division of Entomology, 1969–70. Pp. 100. (Canberra: CSIRO, 1971.) [197

Indian Forest Records (New Series), Forest Pathology. Vol. II, No. 10: Cultural Diagnosis of Indian Polyporaceae. 2. Genera *Fomes* and *Trametes*. By B. K. Bakshi, Manjusri Sen and Balwant Singh. Pp. 245–276 + 11 plates. (Delhi: Manager of Publications, 1970.) Rs. 3.85; 45p; $1.39. [197

The Structure and Content of Agreements between the Agency and States Requites in Connexion with the Treaty on the Non-Proliferation of Nuclear Weapons. Pp. 29. (Vienna: International Atomic Energy Agency, 1971.) [197

Institut Royal Météorologique de Belgique. Publications Série B, No. 64: Qu'est-ce que la Serein? Par L. Dufour. Pp. 18. (Bruxelles: Institut Royal Météorologique de Belgique, 1971.) [207

International Labour Office, Geneva. Occupational Safety and Health Series. No. 21: Ergonomics and Physical Environmental Factors. (Proceedings of a Symposium organized by the International Labour Office and the Ente Nazionale Prevenzione Infortuni in Rome, Monte Porzio, 16–21 September 1968.) Pp. v + 426. (Geneva: International Labour Office, 1971.) [207

Instituto Gulbenkian de Ciência. Centro de Economia e Financas. The Economics of Educational Costing—Inter-Country and Inter-Regional Comparisons. IIIB: Conclusions, Bibliography and Index. By Manuela Ferreira Leite, Patrick Lynch, Keith Norris, John Sheehan and John Vaizey. Pp. 58. (Lisboa: Instituto Gulbenkian de Ciência, Centro de Economia e Financas, 1970.) [207

The Mineral Industry of New South Wales. No. 46: Rhenium. Compiled by D. P. Watson. Pp. 15. (Sydney: Department of Mines, Geological Survey of New South Wales, 1970.) 50c. [207

Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 71–10: Publications on the Geology of the Arctic Islands by the Geological Survey of Canada. Compiled by R. L. Christie. Pp. 21. 75 cents. 4 Geological Maps. (Ottawa: Information Canada, 1971.) [217

Annals of the South African Museum. Vol. 56, Part 5: The Cranial Morphology of the Dicynodont Genus *Lystrosaurus*. By M. A. Cluver. Pp. 155–274. R10.50. Vol. 57, Part 9: Species List of South African Freshwater Ostracoda with an Appendix Listing Museum Collections and Some Further Determinations. By K. G. McKenzie. Pp. 157–213. R4.00. Vol. 57, Part 10: The Family Sergestidae in the Waters Around Southern Africa (Crustacea, Decapoda, Natantia). By Brian F. Kensley. Pp. 215–264. R5.00. (Cape Town: South African Museum, 1971.) [217

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NATURE Volume 234 NOVEMBER 19 1971

How Much is Enough?

THE most respectable of all numbers games is the prediction of population, as in the United Kingdom. Unlike other forms of gaming, bingo or blackjack, for example, trying to tell how many young people will need desks in schools ten years ahead, or how many older people will need hospital beds in which to be sick, tends to be invested with all the propriety of social purpose. A demographer is a social scientist, not a gambler—that, at least, is what his friends and employers say. The latest attempt to estimate the future population of the United Kingdom, *Population Projections 1970–2010* prepared by the Government Actuary (HMSO, £1.20), goes a long way to suggest that the truth may be on the other side of the coin, and that the time has come for those who would predict the future population of a nation to throw a handful of dead leaves in the air and then count the number falling right side up.

The Government Actuary (a statistical analogue of an astronomer-royal not to be confused with the head of the British Government's Statistical Service) has on this occasion set out to estimate the population of the United Kingdom and the several parts of it (Ulster included) in the next forty years. Up to a point, the exercise makes sense, for more than half of the people who will still be alive in Britain in AD 2000 are alive already. Many of them are even middle-aged. To that extent, it is easy enough to estimate the population of old people's homes at the turn of the century. Unhappily, it is much more difficult to estimate how many young people there will be. Especially now that it has become unfashionable for the parents of large families to declare in public how great a claim they have made on future resources, and with women's liberation just around the corner, not even a Government Actuary can be sure what he intends by a population prediction for the year 2000.

The latest prediction is not merely uncertain but also as unoriginal as anybody could wish. For the United Kingdom as a whole, the population is expected to increase steadily from 55.8 million in 1970 (halfway through the year) to 58.9 million in 1981, 62.3 million in 1991 and 66.5 million in 2001. In other words, the increase of population is estimated to be about 20 per cent in the course of the next thirty years. In the circumstances, it is only proper to ask how accurate these estimates may be.

In the thirty years between now and the end of the century, rather more than 20 million people will die. Emigration will account for about 2 million more even if the growing political integration in Western Europe does not further stimulate the tendency for people born in Britain to earn their living abroad. During the same period and on the assumptions which the Government Actuary has made about the future fertility of the United Kingdom, something like 25 million people will be born or will immigrate into the United Kingdom. Quite apart from the uncertainties which there must be about the future trend of fertility, the balance of emigration and immigration may be a source of great error—the 1971 census shows an error of 500,000 on this score in the past decade. In ordinary life, in a physics laboratory for example, nobody would complain if the Government Actuary had thrown up his hands in the face of these uncertainties and had declared that forecasting of the population of the United Kingdom thirty years from now would be impossible. The demographers, unfortunately, expect no less of themselves and their colleagues. The trouble, of course, is that the errors in such a process are so great that the forecast is in part at least a kind of guess.

Quite understandably, the Government Actuary bemoans the way in which the fertility of the women of the United Kingdom has fluctuated in the past few years. In the space of a quarter of a century, the number of births each year has fluctuated between less than 800,000 and rather more than 1 million.

In the mid-1960s, the official demographers were so impressed by the rapid growth of fertility that they were seduced into estimates of the population of the United Kingdom amounting to close on 80 million by 2000—estimates so alarming that they have since become a part of the popular mythology of population growth. In the event, not merely fertility but the number of births each year in the United Kingdom has since fallen steadily, yet even now the latest estimate of population is based on the assumption that this tendency will be reversed forthwith. In these circumstances, very few of those who put money on racehorses would be persuaded that it can be sensible to back the most bullish of the estimates which the Government Actuary has put forward. It is at least as good a bet that the population of the United Kingdom will be the same at the end of the century as it is at present. If there is a change, it will most probably consist of an increase of the proportions of old people and a corresponding decrease of young people.

The moral, which should be heeded not merely by the Government Actuary but by the three registrar-generals of the United Kingdom, not to mention such organizations as the Census Bureau in the United States and the Population Commission of the United Nations, is that there are serious limits on attempts to forecast the population of countries, regions or the world as a whole. It may be possible in advanced societies, where the death rate is reasonably predictable, to estimate the numbers of schoolchildren three or four years ahead or the numbers of old-age pensioners fifty years ahead, but the estimation of how many young people there will be by the end of the century requires a much better understanding of the motives which persuade couples in advanced societies to have children or to forswear them as well as a certain amount of luck. As it happens, this is the most notoriously unreliable parameter in the demography of the future. In the circumstances, might it not be a great saving of public funds if the Government Actuary and the other organizations which are tempted to follow in these inelegant footsteps—on this occasion, the Actuary has not even put forward an estimate of the extent to which he thinks his estimate may be uncertain—were to settle for more modest but more realistic goals in forecasting the population?

Science was a Sacred Cow

SIR FREDERICK DAINTON, playing Caesar's wife as always, gave no tangible sign in his Fawley lecture last week of what his report on the administration of civil science will have to recommend when it is published (as the Government now promises) before the end of the year (see page 118). That is perhaps as well, for there is every prospect that the forbidden fruit, when eventually it is tasted, will be a disappointment—not so much a programme for change as a recipe for preserving the present state of affairs.

The strongest part of Sir Frederick's declaration was that in which he pleaded for a better appreciation of the place of science in the enterprise of modern civilization. In the long run, it may be more important that people should understand what value there is in science than that there should be a radical programme for the reconstruction of organizations such as the Science Research Council, the Council for Scientific Policy and even the University Grants Committee. What is the value of it all? And how does it come about that throughout the industrialized world, scientific enterprise is in the doldrums?

Much of what has happened is intrinsically a part of the scientific enterprise itself. Sir Frederick was right to say as much. The temper of science has changed enormously in half a century. The change consists simply in the organization of working scientists into teams and their congregation around important and expensive items of equipment. But it also follows that those who pay for the expensive apparatus, usually taxpayers, should increasingly ask difficult and obscure questions about the extent to which the community which pays the piper is able or even competent to call the tune. The endless preoccupation with the machinery for the administration of civil science, red herring though it may be, is one symptom of the public determination to extract what benefits there may be in an item of public expenditure which falls not far short of three per cent of the gross national product in countries such as Britain and the United States. It would of course be better for the community as well as for professional science if these questions could be directed more accurately to the problem of making the best use of civil science.

Sir Frederick Dainton has a large part of the answer, for in his address last week he quite properly took the universities to task for failing to take a proper view of their chief function, the training of young people in science and related crafts. Two manifestations of this failure have been especially prominent in the past few years. First, university teachers and their students have fallen into the habit of bewailing the difficulty of finding jobs in professional science, which amounts simply to a complaint about the difficulty of finding jobs for science graduates in research, development or higher education. Second, there is a growing torrent of complaint from employers and potential employers that the instruction offered to undergraduates in science is not such as to equip them for a wider life. Universities are still trying to provide students of science with training of the kind best suited for the winning of a Nobel prize. Yet what the students need is a blend of competence and knowledge that will allow them to function well not merely as academics but in more practical jobs as well.

How is this to be achieved? Attempts at more flexible curricula have merely scratched the surface. What has become of the brave declarations by the Science Research Council that it would encourage radical innovations of the curriculum? A number of universities have broken a little new ground, but there is not much of it. Yet is it not in the immediate interests of the scientific enterprise that the quality of higher education in science should be rapidly changed? And how can this be done if the research councils still spend all their money on research as such and not on pedagogy in the widest sense?

Externally, there are still more serious problems to contend with. For lack of argument to the contrary, the impression has grown up that science is not so much a good thing as a bad thing. It tends to be forgotten that the "science" which has provoked the world population growth consists of the avoidance of avoidable disease, that the prosperity held responsible for air pollution and other evils has powerfully narrowed the gap between the rich and poor in advanced societies and that those societies now have a far greater capacity to help developing nations. To be sure, it remains to be seen whether in the few decades the full promise of what now appears possible will be realized, but there is at least a case for asking that professional scientists should play some part in advocating such a course. Sir Frederick Dainton was right, last week, to remind them of where their duty lies.

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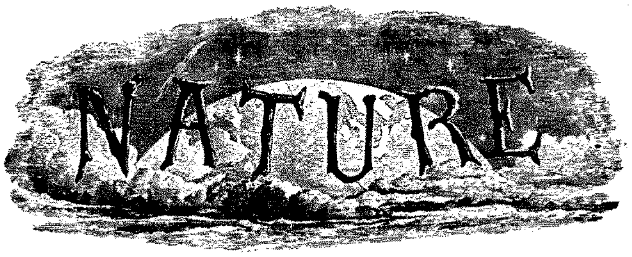
100 Years Ago



It remains to be seen whether the Council will consent, at the bidding of the Senate, to rescind the regulations which they themselves freely passed in 1869, with the sanction of the Senate, viz. :—

> "Women shall be admitted to the study of medicine in the University. The instruction of women for the profession of medicine shall be conducted in separate classes, confined entirely to women. The professors of the Faculty of Medicine shall, for this purpose, be permitted to have separate classes for women. All women attending such classes shall be subject to all the regulations now or at any future time in force in the University as to the matriculation of students, their attendance on classes, examination, or otherwise."

Any proposal for mixed classes of both sexes in purely medical subjects excites so great a repugnance both among the teachers and students of medicine that it would be extremely unwise to press it; but it will be observed that no such question has been raised here, and no such request has ever been made by the lady medical students

From Nature 4, 58, *November* 23, 1871.

OLD WORLD

SELECT COMMITTEE

Cash for Computers

THE establishment of a computer purchasing board is recommended to resolve the involved and intricate process by which the British government buys computers. In a report published yesterday the Select Committee on Science and Technology calls for an end to the present system that involves collaboration with several departments before an order is finally placed by the Stationery Office and it recommends that the purchasing board be directly responsible to parliament through the Civil Service Department (*The Prospects for the United Kingdom Computer Industry in the 1970s*, HMSO, £0.47).

A further recommendation is that the government maintains its present policy of giving preference to the British computer industry as it has done to ICL but that the system should be based differently to that operated at present. In particular, more government aid should be given in the form of grants and development contracts—and less at the tendering stage. This latter system has aroused a great deal of furore in past years, with IBM and Honeywell complaining that even though they contribute to the balance of payments in Britain they are unfairly discriminated against, claiming that they have to tender 25 per cent lower than their British competitors to land a contract (see *Nature*, **230**, 4; 1971).

To implement a policy of government support for the computer industry the committee recommends the establishment of a computer research and development board through which all government support for the computer industry will be channelled. The board will have to decide on the amount of support to be given to companies and in a proposed set of criteria companies whose parent bodies are outside Britain can qualify for support. In awarding contracts, however, the committee recommends that price and performance should be the prime consideration and that in some instances these should have overriding priority. These suggestions should go a long way towards mollifying companies such as IBM and Honeywell and should ensure that ICL will continue to be a viable entity.

The committee comes out strongly for an independent British computer industry and it says that the industry should not become dominated by foreign technology. To ensure this the committee says that a considerable research and development effort is required to the tune of at least £50 million a year supplied by the government. It considered that apart from the £13.5 million that the government had already injected into ICL the support of the industry has been "derisory". The committee also pointed out that the original purpose of this grant was to improve the research and development facilities of the company but in fact it had gone to improve the financial resources of ICL after the merger of ICT, English Electric Computers and the computing interests of Plessey. There is at present no assurances that further aid will be given to the industry—which has amounted to only £3.2 million in six years—and the committee is concerned that even the present level of support could be cut.

The report comes out strongly in favour of government departments making use of independent software houses. The committee argues that the use of independent companies to supply computer programs and services will make for efficient use of government computers as well as strengthening the computer industry in Britain.

GRADUATE EMPLOYMENT

Significant Statistics

MORE first degree graduates of British universities took up further academic study or research in the pure sciences in 1969–70 than in 1968–69 but the number of men embarking on applied science research was smaller than in the previous year (*First Employment of University Graduates, 1969–70*, University Grants Committee, HMSO, £0.68).

The increase in the proportion of pure science graduates entering research during 1969–70—from 28.7 to 29.4 per cent for men and from 14.8 to 15.3 per cent for women—contrasts with a reduction in the percentage of all graduates entering research or further study which has been evident since 1964–65. Then, of the 27,549 first graduates of British universities, 5,682 students continued with further study whereas in 1969–70, 7,149 out of 47,584 graduates remained at university. Since 1966–67 the number of students entering research or academic study has remained substantially constant at a time when the total number of graduates has increased by more than 11,000.

The percentage of male applied scientists starting on research work decreased from 14.4 per cent in 1969 to 12.7 per cent in 1970, whereas the proportion of women graduates in applied science who started research increased slightly in the same period. The number of applied science graduates increased to 19.0 per cent in contrast to the number of graduates in pure science, which continued to drop—in 1969–70, 29.1 per cent of all degrees were granted in pure science compared with 30.1 per cent in 1968–69.

More than eleven thousand students graduated with higher degrees in 1969–70 of which 64.6 per cent were in the sciences. Of the British students who obtained higher science degrees more than 22 per cent went into industry and 13.3 per cent went overseas. By contrast, only 7.9 per cent of arts higher degree graduates sought their first employment abroad.

INDUSTRIAL RELATIONS

Professionals' Plans

PLANS are firmly afoot to found a Confederation of Professional and Executive Associations. The confederation is essentially the brainchild of UKAPE, the United Kingdom Association of Professional Engineers, whose general secretary, Mr Kenneth Peplow, said last week that he hoped to see CPEA fully active by January 1, 1972. The aim of the confederation will be to provide the machinery for professional bodies to express their viewpoint on matters which affect them. Mr Peplow says that he has received about 90 enquiries from various bodies—not all of them professional associations—but that the founding members of CPEA will be UKAPE, the Association of Supervisory and Executive Engineers and the scarcely formed Association of Professional Scientists and Technologists (see *Nature*, **233**, 440; 1971).

Mr D. B. Sweaney, general secretary of the ASEE, said this week that the confederation would be a non-militant and non-political body with which employers could deal in wage negotiations and other matters as the member associations would give the confederation full negotiating rights on their behalf. One qualification for the confederation is that the associations must have a professional code of conduct and ethics, and it is this the sponsors feel that demarks associations from other trade unions. UKAPE and ASEE are fully in favour of the scheme, although Mr Barry Henman at APST was more cautious. APST has only been a corporate body for a few weeks and its initial recruiting drive is being launched this month, so that while APST "values a common front [with other professional associations] the decision to join must be decided by the governing body of APST and this has not yet been done". APST holds basically similar aims to UKAPE and its organization has no doubt been accelerated by the realization among scientists that once the new Industrial Relations Act comes into force scientists in industry will definitely be on the employees' side of the fence when it comes to wage bargaining.

The plans for the confederation are ambitious—Mr Peplow hopes it will come to include all professional associations—but the strength of the three involved so far is not great—UKAPE has 11,000 members and ASEE about the same. Reaction from some quarters is far from enthusiastic — a spokesman for the TUC said "there is no need for it, we cater for professional bodies here", and the reaction of Mr C. Cooper, deputy general secretary of the Institution of Professional Civil Servants, was that the scheme was "grandiose" and unnecessary as individual associations are quite capable of negotiating with employers and he doubted if there would be much recognition for the confederation.

METALS

Continuing Uncertainty

International Nickel, the largest producer of nickel in the world, is being forced to cut down production because of a sharp decline in sales during 1971 and it seems that a cycle which started in 1966 when demand for nickel first began to outstrip supply has come full circle. International Nickel is now planning to reduce its output by 15 per cent by early 1972.

The nickel shortage of a few years ago was exacerbated by strikes at most of the principal mines in Ontario, Canada, which lasted for several months at the end of 1969. International Nickel was not the only company involved and Falconbridge—the third largest nickel producer in the world—was also badly affected. At that time, the output of International Nickel dropped to about 30 per cent of its previous level (£500 million a year) and production by Falconbridge was almost completely halted. Towards the end of 1969, the price in the free market (in which only about 10 per cent of the world's nickel is sold) rose to a level about seven times higher than the so-called producer price (£1,220 a metric ton) at which large companies like International Nickel sell their products. Users of nickel at that time could buy rationed quantities of nickel from large companies at the producer price or greater amounts in the free market at inflated prices.

Now the producer price is £1,246.50 a metric ton and the free market price is slightly lower than this. But the demand for nickel—more than 40 per cent of it is used in the production of stainless steel—has fallen off because of the poor economic climate. Nickel consumers now see that world nickel supplies are plentiful and are happy to allow their own stocks to fall to quite low levels.

There are at last some signs that the sales of aluminium in Britain are picking up after a disastrous nine months for the industry that has seen the rate of growth of sales drop to around 1 per cent. This has led to stockpiling by the manufacturers and a slowing down in the time scale of bringing new smelters into operation. A spokesman for the British Aluminium Company said last week that it would be eighteen months before the situation was rectified, although it would be longer before the world-wide rate of expansion would be restored to its pre-1970 rate of 8 per cent.

In spite of these difficulties the posted price of aluminium remains at the 1970 price of £257 a metric ton although this hides the real situation where aluminium dealings are currently being conducted at up to £70 below this price. The stability in the price is one of the aluminium companies' selling points and the inroads made into the sales of copper in Britain during the past five years can be seen in the table.

Until recently Britain imported most of the 400,000 tons sold annually because of the large amount of electricity needed—16,000 to 18,000 kilowatt hours—to produce a ton of metal from alumina. Four years ago the government in an attempt to reduce Britain's balance of payments offered inducements to aluminium companies to build smelters in Britain. These plants are now becoming operational and when fully operational they should produce 300,000 tons a year that will reduce Britain's dollar drain by up to £40 million. The companies themselves will also save on import tariffs when Britain enters the European Economic Community.

The copper market is in its steadiest state for years. After the gradual decline of the past year the price seems to have settled at about £420 on the London Metal Exchange and no significant changes are expected in the near future.

The copper market is well known to be an early indicator of economic trends, and the low level of the market, compared with last year when the price at one stage reached £749 a metric ton, is partially accounted for by the depressed state of the world economy. For the first time in some years there is an excess of supply over demand, partly due to new copper mines coming into production which were planned when copper prices were high and supplies were low in 1968 and 1969. The London Metal Exchange, which controls the price of 60 per cent of the world's copper, has reserve stocks at the moment of more than 132,000 tons, the highest ever, and until these begin to fall the price is unlikely to rise a great deal. It is thought in many quarters that a price of about £500 a metric ton can be expected by the middle of next year as it is assumed that the American economy will be re-inflated when the presidential election campaign begins.

Copper is the most volatile metal market for a number of reasons. The countries which supply the bulk of the world's copper—Zambia, Chile, Peru and the Congo—are not renowned for their political stability, and the copper industry seems to attract more than its fair share of strikes. Again, copper is not protected from speculators in the way that other metals are. Aluminium and nickel, for instance, are largely sold at the price the major producers agree between themselves and although price changes are usually large, it nevertheless remains constant for longish periods.

Table 1 Metal Data 1966-71

Metal	Annual consumption UK		Price per tonne		
	1966	1970	1966	1970	1971
	'000 metric tons			£ sterling	
Aluminium	366.0	404.2	193	257	257
Nickel	34.4	34.7	691	1,268	1,268
Copper	592.5	546.5			418*†

* Average figures. † Average price for October.

SCIENCE POLICY

Dainton on Science

Sir Frederick Dainton, chairman of the Council for Scientific Policy, believes that the current disenchantment with science arises because science was oversold in the postwar years and because there is at present a "long term distaste if not active revulsion from science". These views were expressed by Sir Frederick last week at the University of Southampton when he gave the annual Fawley lecture on "Science: Salvation or Damnation".

Sir Frederick is nevertheless optimistic about the future even though he openly admitted that his lecture did "little more than list many maladies from which we suffer". He believes that "knowledge is the best weapon to combat fear and therefore that if science is taught and practised imaginatively and with a sense of social responsibility, the present disenchantment with it will not long persist".

The body of Sir Frederick's address reviewed the nature and development of science from the carefree days when a chemistry professor could ask his assistant to bring in his laboratory on a tray to the present, where in Britain £1,000 million a year is spent on research and development. Sir Frederick is being realistic, however, when he states that historians will probably regard the 1970s as the time "when near adulation of science gave place to feelings ranging from grave doubts to at worst a neo-Luddism based on fear".

Sir Frederick is emphatic that the clock cannot be put back to remove the current disillusionment with science, and he stressed that "to attempt to stop any further scientific research is both wrong and impracticable". Sir Frederick also felt that it is impracticable to stop work on branches of science that "serve the baser needs of man and nation" because one cannot predict in advance the outcome of research. On accepting that scientific work must continue Sir Frederick asked whether the scientist has a moral right to suppress his findings and to stop pursuing a particular topic. He suggested that the scientist should weigh up the advantages and disadvantages of his work and make this knowledge known.

When Sir Frederick was talking on the prospects for science in Britain in the 1970s his listeners were possibly most attentive. But with his review of the future of the research councils yet to be published Sir Frederick merely defined the problem. He asked whether research within the universities should keep pace with the expansion in higher education and whether research should be concentrated in "centres of excellence". Sir Frederick did not believe that such centres would involve the risk, as feared by some people, of not producing good scientists from the less favoured institutions provided the present system of both University Grants Committee support and research council support is maintained. He did issue a warning, however, that a shortage of money will possibly require more inter-university collaboration in research.

Sir Frederick also mentioned collaboration between scientists and social scientists. He said that it was almost certain that a much closer relationship must develop between science policy, social economic affairs and government policy but there was no clear way how this relationship is to be achieved.

INDUSTRIAL RELATIONS

Battle or the War?

THE majority ruling of three Appeal Court judges last week means that Mr Jack Hill has won his battle with C. A. Parsons, the Newcastle engineering company who dismissed him for refusing to change his trade union. It remains to be seen, however, whether the United Kingdom Association of Professional Engineers (UKAPE), of which Mr Hill is a member, has won the war.

The appeal was against Mr Justice Brightman's decision earlier this year that under the law as it stands he could not prevent Parsons from dismissing Mr Hill for refusing to leave UKAPE and join DATA—the Draughtsmen's and Allied Technicians' Association—who, by working to rule twice and striking once, won a closed shop agreement from the company (see *Nature*, **233**, 5; 1971). When Mr Hill refused to join DATA, he and thirty-seven other engineers were given a month's notice. Mr Hill sued the company for wrongful dismissal and both he and UKAPE saw the resultant action as a test case.

Not so the company apparently. The day after the appeal decision Mr Kenneth Peplow, the general secretary of UKAPE, said that he had been informed by the company's solicitors that UKAPE will have to fight the remaining cases individually, but at the moment Parsons will not confirm that further action will have to be taken.

If thirty-five more actions are needed (two engineers have left the company since July) then Mr Peplow sees it as "a campaign of spite", but adds that he cannot believe it has been generated by the company. "It makes one wonder," he said last week, "what influences and pressures have been brought to bear so that a company is no longer in control of its own destiny."

Mr Harry Smith, DATA's public relations officer, said this week that they are "disappointed", but he was not prepared to commit himself on what DATA expects of the company until the association had met its legal advisers yesterday and representatives of the company next Tuesday, but they are clearly reluctant to accept last week's ruling as a test case.

Whether it is a test case may prove to be an academic question, however, as any writ issued now is unlikely to be heard before the relevant clauses of the Industrial Relations Act become law early next year. As UKAPE have registered as a trade union under this act, and DATA have deregistered, then it would appear that UKAPE will be in a stronger legal position.

UKAPE's determination to see this through is reflected in its appeal for a defence fund of £1 million launched last week. UKAPE has 11,000 members but is hoping that it can raise £5 a head from the 200,000 engineers in Britain. UKAPE is determined to fight for recognition wherever it is denied, according to Mr Peplow, and the new act could give it the opportunity to do so effectively. Mr Peplow emphasizes that UKAPE is determined to act legally and to adhere to the code of ethics that it maintains is the distinguishing feature between professional associations and trade unions, but it is equally determined to protect what it sees to be its rights. Companies other than Parsons may have to face up to UKAPE soon.

STEEL

Rationalizing Research

THE British Steel Corporation's efforts to rationalize and coordinate the research performed in its own laboratories is coming to fruition, according to a report which surveys the work in progress (*Steelresearch 71*, British Steel Corporation; 1971).

Steelresearch 71 is the first comprehensive annual review of the research activities of the corporation, which now cost about £9 million a year. As well as describing the work of the laboratories attached to the corporation's six product divisions, the report also covers the activities of Bisra which, since 1967, has gradually evolved from an autonomous research association into the corporate laboratories of the British Steel Corporation. The decision that a separate annual report is no longer to be published is a clear sign that the amalgamation of Bisra into the corporation's research structure is now almost complete. Almost 95 per cent of the £2.7 million spent by Bisra comes from the British Steel Corporation and it now has an important role to play as the central body responsible for research of an innovatory or long-term nature (for example operational research devoted to increasing the efficiency of all aspects of the corporation).

The corporation's other research activities have centred on the product divisions (for example the special steels division and the tubes division) which themselves evolved from the four groups formed on a geographical basis when the corporation was created in 1967. There has inevitably been wasteful repetition of research and during the past year there have been particular efforts to minimize it. Because of their expertise in on-line non-destructive testing, for example, the laboratories of the tubes division at Corby have assumed special responsibility for the development of these techniques; the Swinden laboratories of the special steels division at Rotherham have, for similar reasons, been designated a centre of expertise in the machinability of steels.

The reorganization of research activities reflects the work of the research committee whose wide ranging brief is to "review and coordinate the research and development work of the divisional and corporate laboratories". A spokesman for the British Steel Corporation said this week that further rationalization along similar lines could be expected when other areas have been identified in which the drawing together of projects would be fruitful.

The corporation also spends £100,000 a year in universities and a further £60,000 a year on about sixteen fellowships, usually tenable for two years.

NEW WORLD

Controlled Optimism for Fusion Power

by our Washington Correspondent

CLEAR signs of optimism for the prospects of producing marketable power from controlled nuclear fusion emerged in Washington last week. Indeed, one expert on the subject even went so far as to declare that "progress towards power through nuclear fusion is now limited by resources available to the programme rather than by scientific obstacles".

Although such unqualified optimism may have been tinged to some extent by the fact that the remarks were addressed to members of the Joint Committee on Atomic Energy—the Congressional body that holds the purse strings for the controlled thermonuclear research project in the United States—a string of witnesses before the committee produced good evidence of progress with which to back up their assertions. Nobody was of course prepared to say that fusion power is just around the corner, but almost every witness before the committee felt confident enough to predict that the feasibility of producing power from nuclear fusion will be demonstrated by the end of the decade.

The logical extension of this optimism is that decisions will soon have to be taken on whether the predictions should be backed by large increases in funds—a situation which in itself demands some potentially painful ordering of priorities within the controlled thermonuclear research programme. But exactly what level of funding is now needed, and in particular how it should be applied, is an open question.

Members of the Joint Committee on Atomic Energy were anxious last week to solicit from their witnesses some idea of how soon power from nuclear fusion would be able to compete economically with power produced by other means. That question, indeed, emerged as the central point of interest to the committee, which was clearly trying to use the advent of marketable fusion power as the base point by which to judge the level at which funding should in future be authorized. Not surprisingly, the committee received a spread of dates, ranging from about 1990 as the most optimistic, given a very high level of funding, to "some time before 2020". The consensus was, however, that it is probably realistic to talk in terms of producing commercial power from fusion plants by the year 2000 although the actual date will depend in very large measure on funding.

The fact that scientists deeply involved in the research programme are now willing to talk, even in vague and handwaving terms, of the possible date of application of fusion power, when the feasibility of even producing such power has yet to be demonstrated bears witness to the considerable theoretical advances that have been made during the past few years. Indeed, it can now be safely said that the point will shortly be reached at which very large equipment will be needed to determine whether the advances made in the laboratories hold up on a large scale.

The point was very clearly brought out last week that there are essentially three milestones which must be passed on the road to thermonuclear fusion power. The first is the demonstration of scientific feasibility—the immediate goal towards which present research is directed—then comes the building of a demonstration plant to test whether the processes developed in the laboratory can indeed be applied to energy production, followed by prototype and commercial power plants. For nuclear fission in the United States, the gestation period between proof of scientific feasibility and commercial production was some 25 years, but last week the scientists engaged on the research were predicting that the comparable time lag for fusion could be cut down to about 15 years with sufficient funding.

As for the demonstration of scientific feasibility, the chief objective is to heat a plasma fuelled by deuterium or a mixture of deuterium and tritium to a very high temperature, and confine it in a space free from contact with any material walls long enough for a fraction of the fuel to react. That, in essence, is the required operation, but so far no techniques in the laboratory have come close to containing the plasma long enough, or heating it to the required temperatures. In the United States at least, the chief thrust of the research over the past few years has been directed towards confining the very hot plasma by means of magnetic fields, and it is this research which is now producing the promising results.

Research aimed at finding methods for confining the very hot plasmas has in the past followed four different paths. At the Lawrence Livermore Laboratory and the Oak Ridge National Laboratory, plasma physicists have been studying confinement by so-called magnetic mirror devices, which essentially hold the hot plasma in a specially shaped magnetic field. The problems come when the plasma is sufficiently dense to argue back at the field, and diffuse across it so rapidly that it is confined for too short a time to react. The theoretical understanding of the instabilities which cause the rapid diffusion has, however, reached such a state that Dr R. F. Post, who is in charge of the project at the Lawrence Laboratory, told the committee last week that "I'm optimistic about the prospects for controlling them . . . if we can in fact demonstrate their control we should be ready for scientific feasibility tests".

Mirror devices, which work with plasmas of relatively low density, need to contain the plasma for a relatively long time to meet the criteria necessary for scientific feasibility—of the order of 1 s. The devices which have made the headlines recently, the tokamaks and stellerators, also employ magnetic fields for confining the very hot plasmas, and work with slightly denser plasmas than the mirror devices. In some respects, the two types of device have similar characteristics, but the tokamaks confine the plasma in a toroid. The chief breakthrough with these machines came in 1969, when a large tokamak in the Soviet Union produced an unexpectedly large heating.

The other two approaches consist of techniques for suddenly compressing a plasma by a magnetic field (the so-called "pinch" machines), and of rapidly heating a solid block of fuel by means of a laser. Proponents of each method for reaching the criteria for achieving power from fusion presented evidence last week to show that they are close to the breakthroughs needed to demonstrate scientific feasibility, and this is one reason why those in charge of planning the controlled thermonuclear research programme in the United States will soon have some difficult choices to make. The problem is that to take any of the methods to the stage of demonstrating feasibility will require the expenditure of large sums of money on big machines, and, sooner or later, one or two of the approaches are bound to fall by the wayside while the others are taken to the next stage. That, of course, would mean a dereliction of ambition in many laboratories.

Another problem for the planners is that reactor designs associated with each of the methods now being investigated would have individual characteristics, and it is therefore a potentially wasteful process to concentrate too much on power plant design, at least until the scientific feasibility stage is almost reached.

All the witnesses last week emphasized, however, that it is still too early to decide which horses to back, and the policy of keeping all options open is the correct one at present. Whether or not the Joint Committee on Atomic Energy is willing to increase its widely spread bets is, however, a moot point, but it was clear last week that key members of the committee are more ready at present to back the breeder reactor.

PESTICIDES

A Few Loopholes

by our Washington Correspondent

IF a bill passed last week by the House of Representatives finds its way to the statute books, the federal government will for the first time have the power to regulate and control the manufacture and use of pesticides. At present, federal controls on pesticides apply only to their labelling and to their sale across state lines. But the squeals of anguish that might be expected from the chemicals companies and from the powerful farming lobby at such a prospect have been drowned by the protests of environmentalists.

Environmentalists charge, with some justification, that the bill is a toothless shadow of legislation introduced into Congress earlier this year by the Administration, and that it contains some important loopholes for chemicals manufacturers. Spokesmen for the chemical industry are, however, much less willing to comment on the bill except to admit that it will be easier to live with than the Administration's original proposals.

In its present form, the bill establishes the important concept that the Environmental Protection Agency should have the right to inspect manufacturing facilities, which would be registered with the agency, examine records and take samples. And, as far as pesticide use is concerned, the bill requires that all pesticides be registered with the EPA, which would classify them as either for general use or for restricted use. As for enforcement, controls on the manufacture or use of pesticides would be enforced by the states, and the EPA's regulatory arm would be stiffened by powers allowing it to bring court injunctions, impose civil penalties, seize unlawful products or bring criminal charges against violators.

There are also provisions in the bill for public comments on any action taken during registration of a pesticide, or during the proceedings that follow cancellation or suspension of an agent's registration. Questions of scientific fact would be referred to the National Academy of Sciences, in much the same way as under the existing law, but the new bill also allows a scientific review to take place in conjunction with a public hearing, while the existing law separates the two procedures, thereby causing undue delay.

All that, of course, raises few objections among environmentalists, for it considerably stiffens existing laws, and allows for at least a minimum set of standards to be enforced on the manufacture and use of pesticides. In that respect, it represents a considerable step from the present law which only gives the federal government powers to enforce labelling standards, and to ban or restrict the sale of pesticides between different states. But environmentalists are concerned both by other provisions that found their way into the bill, and by some concessions that chemicals manufacturers managed to wring from the Agriculture committee before it reported the bill to the House.

One bone of contention is that the Administration's original proposals called for the classification of pesticides into three categories, the last one being for use by permit only. This was deleted by the committee on the grounds that it would be too difficult to enforce, and means that some of the most toxic chemicals would instead come under the less rigorous controls imposed on the "restricted use" category in the present bill. Another proposal which has irked critics of the chemicals industry is the provision written into the bill for paying federal money to manufacturers who are left with considerable quantities of pesticide on their hands in the event that a pesticide's registration is cancelled. This provision was bitterly attacked when the bill was debated in the House, on the grounds that the government would effectively be paying industry for its own mistakes. But in the event, an amendment to delete the provision was rejected by a wide margin.

The Agriculture committee also wrote into the bill the provisions for scientific review by committees of the National Academy of Sciences. According to one member of the committee, this provision was put into the bill at the insistence of the Environmental Protection Agency, and the committee held a special session to draft it into the bill. Congressman John Dow, chief spokesman against the bill on the floor of the House, and also a member of the Agriculture committee, insists, however, that such a scientific review can be effectively used by chemicals manufacturers to hold up proceedings, and moved to have the provision deleted from the bill. His amendment was rejected by a voice vote, however. The National Academy of Sciences itself would also have been happy to see its name removed from the bill, since such a provision tends to erode its independence from the government.

All these arguments are likely to have a second showing early next session, when the Senate should be voting on companion legislation. So far, a Senate committee has conducted hearings on the Administration's bill, but no bill has been sent to the Senate itself.

HEALTH MANPOWER

Plugging the Gap

by our Washington Correspondent

THE House of Representatives last week sent to President Nixon a bill providing $2,900 million over the next three years for the training of doctors. The bill is the product of protracted negotiations in a conference committee which was set the difficult task of reconciling differences between fundamentally different bills passed in August by the House of Representatives and the Senate. Chief intent of the bill is to increase the numbers of doctors in the United States, particularly in areas where there are substantial shortages.

The bill now awaiting the President's signature, although it involves expenditures considerably in excess of the modest proposals sent to Congress earlier this year by the Administration, is expected to meet with little resistance in the Administration. The bill authorizes construction grants to medical schools, totalling $225 million in 1972, $250 million in 1973 and $275 million in 1975. Medical schools would also receive federal funds on the basis of their student enrolment, with grants of $2,500 for each student in his first, second and third year, $4,000 for students in their fourth year, and as an incentive for schools to shorten courses, the bill provides for the schools to receive $8,500 for every student in the final year of a three-year course.

Another incentive for existing schools to step up their output of medical students is a provision in the bill which seeks to make a substantial grant to colleges which usually provide two-year courses in basic medical science. Such schools that convert to four-year medical schools will, under the terms of the bill, receive grants of $50,000 multiplied by the numbers of medical students enrolled in their first third year class. As for student support, the bill set aside $50 million next year, rising to $60 million in 1974 for loans to students in the health professions.

The House version of the original bill was produced by the Interstate and Foreign commerce subcommittee, under the chairmanship of Paul G. Rogers, while the Senate version was sponsored by Senator Edward M. Kennedy. Both sponsors declared themselves pleased with the conference committee bill, and the final bill received widespread support in both chambers. In the House, where it only collected three opposing votes, only one member was prepared to speak up against it. His chief grievance was that the bill is the first step on the road to socialized medicine.

Short Notes

Alaskan Oil

CONGRESSIONAL aides have hit upon a peculiarly effective technique of bringing controversial suggestions to public attention. It consists of burying them deep in reports almost as though they were not meant to be noticed. A striking demonstration of the effectiveness of the technique was provided last week when a single five-line paragraph in a 100-page report on oil pricing made headlines. The paragraph suggested that there are oil deposits off the southern coast of Alaska that may be as extensive as those on the North Slope, but that the oil companies are not interested in developing them, and that the Department of the Interior is attempting to conceal the extent of the deposits from public view.

Oil companies reacted vigorously to the allegations by suggesting that although there may be oil deposits there, test bores have failed to detect them, and spokesmen for the Department of the Interior have hotly denied the allegations, saying that no preliminary study of the extent of possible deposits in the Gulf of Alaska has yet been made. The Department of the Interior is, however, now studying seismic data it has bought from two oil companies that have surveyed the region. So far, two oil consortia have sunk test bores in the Gulf of Alaska, but both have been abandoned because of damage from heavy seas. One problem with the area is that even if there is oil in any quantity under the gulf, it would be very difficult to extract because of the notoriously bad weather.

House votes Cancer Bill

THE House of Representatives this week passed by a vote of 350 to 5 the bill sponsored by Paul G. Rogers designed to increase the funding for cancer research but to keep it within the National Institutes of Health. The bill now goes to a conference committee where it must be reconciled with a bill passed in July by the Senate designed to set up an independent agency called the Cancer Cure Agency. Although the bills represent a fundamentally different organizational structure for cancer research, both would greatly increase the funding—the House bill calls for $1,500 million to be spent over the next three years, while the Senate bill asks only for such funding as necessary. Rogers said this week that he is confident the conference committee will agree to keep cancer research in NIH.

Water Pollution

ANY illusions about there being no votes in sewage were quickly shattered last week when it became known that the White House is actively lobbying to have Senator Edmund Muskie's water pollution control bill changed during its passage through the House of Representatives. The bill, which was recently passed by the Senate by a vote of 85–0, calls for a rigorous programme to make all waterways in the United States fit to swim in by the year 1985. A central part of the bill is that responsibility for setting and enforcing water quality standards should be transferred from the states to the federal government. It now seems that the White House is trying to give the states some of their authority back. A redraft of the Senate bill is said to have been sent out to state governors to enlist their support, and to demonstrate to them the White House's concern for their interests. Another aspect of the bill that has caused concern is its cost both to the government and to private industry, and the prospects of a White House–industry coalition do not augur well for the chances that the bill will remain intact during its passage through the rest of the Congressional mill.

DES

THE tide of opposition to the use of the synthetic hormone diethylstilboestrol in cattle feeds gained considerable strength last week. The hormone, which is used to promote growth in cattle, has been under attack since it was reported in the *New England Journal of Medicine* earlier this year that the mothers of 13 girls who developed an extremely rare cancer of the vagina had taken the drug to prevent miscarriage. Since then, there has been a suit filed in the district court to ban the hormone from cattle feeds, Senator William Proxmire has introduced a bill into the Senate, designed to bring about the same end, and experts of the UN Food and Agriculture Organization have spoken out against its use. The Food and Drug Administration has finally been persuaded to act—last week it proposed a labelling change that would warn doctors not to prescribe the hormone to pregnant women.

While this furore has been going on, however, it has been reported that DES is an effective contraceptive agent if taken within 72 hours of intercourse.

AEC

THE Atomic Energy Commission's new regulatory procedures and its new-found attention to environmental and safety factors outlined recently by its chairman James R. Schlesinger, are causing administrative upheavals within the AEC. Chief changes are the creation of a new deputy directorship for reactor licensing and the temporary drafting of 30 professional staff to the regulatory division from other parts of the agency. The AEC is now busy sorting through all the petitions from the power industry showing why their plants should not be shut down or construction stopped, while an environmental review takes place.

New Head for NSF

THE nomination of Dr H. Guyford Stever as director of the National Science Foundation, announced this week by President Nixon, brings to the NSF a man who is well versed in the workings of Washington's scientific establishment. Dr Stever, who will succeed Dr William D. McElroy as director of the NSF on February 1, 1972, is a member of the National Science Board and the advisory panel to the House of Representatives Subcommittee on Science and Astronautics. He has also been Chief Scientist to the Air Force, Chairman of the President's Commission on Patent Systems and a member of several federal scientific advisory committees on science and astronautics. Dr Stever is now president of Carnegie Mellon University, a position he has held for the past six years.

A physicist by training, Dr Stever is an expert on aeronautical and space engineering. He received his AB degree from Colgate University and his PhD from California Institute of Technology and was a member of the Faculty of MIT for 20 years before his appointment as president of Carnegie Mellon University. Between 1942 and 1945 he served in the Office of Scientific Research and Development in London. During his time at Carnegie Mellon University, the establishment has undergone some substantial changes including the merger between Carnegie Tech and Mellon Institute which formed the basis of the present university, and it was also one of the first institutions to receive an NSF science development grant.

Dr Stever comes to the foundation at a critical time in its history. For one thing the past year has seen a tug of war between the Administration and Congress over the NSF's programme of research applied to national needs and its support of graduate education. Although the relative funding for the programmes will be worked out during Dr McElroy's directorship, Dr Stever must justify the foundation's budget to Congress next year.

NEWS AND VIEWS

Plutonium-244 on the Earth

One of the most fascinating detective stories in the history of cosmological and cosmogonical science seems to be solved with the publication in this issue of *Nature* (page 132) of the discovery of plutonium-244 in nature. A joint team of scientists from the Los Alamos Scientific Laboratory and the General Electric Company discovered the elusive nucleus in an old Precambrian rare-earth mineral called bastnasite. Everybody had suspected the natural existence of ^{244}Pu by the clues it had left from the early days of the solar system, and now it has actually been found.

The clues in this mystery began accumulating in 1960 when Kuroda suggested that the excess xenon gas isotopes ^{131}Xe, ^{132}Xe, ^{134}Xe, and ^{136}Xe, which he had found in the achondritic meteorite Pasamonte, had resulted from the spontaneous fission of some heavy radioactive nucleus that had a sufficiently long half-life to have been incorporated into the meteorites when the solar system formed and to have remained there until the meteorites cooled and solidified, enabling them to trap the noble-gas fission fragments. Kuroda specifically suggested ^{244}Pu, which has a half-life of 82×10^6 years. Other workers were also able to find a reproducible spectrum of fission-like xenon in other achondrites, where the low concentration of xenon arising from other sources (primaeval xenon) and the high concentrations of uranium, which chemically accompanies Pu, presented favourable circumstances for the detection of this xenon component.

Then two years ago an exceptionally high concentration of this same isotopic pattern of xenon isotopes was found in the uranium-rich mineral whitlockite, from the St Severin chondritic meteorite. The exciting new clue in this case was that this same whitlockite mineral showed, upon etching, an excess of fission tracks; however, it still could not be argued that the fissioning culprit was ^{244}Pu.

A nagging problem throughout these investigations had been that the yields of xenon isotopes in ^{244}Pu fission had never been experimentally determined because of the difficulty in assembling a large enough sample of ^{244}Pu. Thus the mysterious isotope ratio observed reproducibly in meteorites, $^{131}\mathrm{Xe} : {}^{132}\mathrm{Xe} : {}^{134}\mathrm{Xe} : {}^{136}\mathrm{Xe} = 25:88:92:100$, could not with certainty be attributed to ^{244}Pu. Recognizing the importance of these ratios, a team from the Oak Ridge National Laboratory electromagnetically separated 13 mg of ^{244}Pu from large quantities of neutron-irradiated plutonium. After a 23-month wait to allow sufficient ^{244}Pu fission, a Berkeley team confirmed these fission isotopic ratios directly (*Science*, **172**, 837; 1971). This was the final clue that proved that ^{244}Pu existed in the solar system when the meteorites formed. It only remained to detect its small residues in some object today.

The difficulty in finding natural ^{244}Pu is that the solar system formed about 60 half-lives ago, so that the average concentration of ^{244}Pu should be only about $(\frac{1}{2})^{60}$ of its concentration when the meteorites formed! Inasmuch as an upper limit to that absolute concentration would be expected to be only 3×10^{-25} g per gram of earth even if ^{244}Pu were originally as abundant as ^{232}Th, surely an overestimate by a factor near 100, it was clear that the search must be made in some mineral that would have, in the long and complicated chemical history of the Earth, concentrated the plutonium.

Because the chemistry of Pu is similar to the rare earth Ce, the Los Alamos group studied a large inventory of the extractant used by the Molybdenum Corporation of America to purify Ce from old bastnasite ores. The Ce is almost 10^6 times more concentrated in this mineral than its average concentration; and, sure enough, the long sought ^{244}Pu was there too. Although the chemical enrichment of Pu would have to be about 10^8 (that is, about 100 times more concentrated than Ce) above the ^{244}Pu abundance of 7×10^{-27}g/g expected from the meteoritic concentrations of fission xenon, the results seem convincing. With this discovery, ^{244}Pu leaves the category of "extinct radioactivities" and joins ^{235}U in the category of "almost extinct radioactivities".

The cosmological significance of these discoveries is both simple and profound. When the primaeval meteoritic abundance of ^{244}Pu is considered in conjunction with that of ^{129}I, an extinct radioactive species that decays to ^{129}Xe leaving a different xenon anomaly in the meteorites, it can be concluded that about 1.8×10^8 years elapsed from the time when a portion of interstellar gas collapsed into the gas cloud that was to form the solar system and the time when the newly formed meteorites were cool enough to retain noble xenon gas. This well determined interval for the formation and cooling of the meteorites poses a firm challenge to theories of the formation of solid objects. But the implications do not stop there. Because ^{244}Pu, ^{238}U, ^{235}U, and ^{232}Th are all synthesized in comparable amounts in exploding objects, their relative abundances reveal that nucleosynthesis began in the galaxy about $12 \pm 2 \times 10^9$ years ago and occurred continuously from that time until the time the solar system formed about 4.7×10^9 years ago. This age pattern for galaxies must now be regarded as a prime fact for cosmology.

There is, however, another possible interpretation of the Los Alamos discovery. The Los Alamos group acknowledge that heavy cosmic rays may bombard the Earth with a flux such that the average terrestrial concentration of ^{244}Pu would be about 5×10^{-25} g/g. But because the Precambrian bastnasite is, as a mineral deposit, older than 5×10^8 years, the ^{244}Pu concentration would now be only about 5×10^{-27} g/g if it had been deposited on the Precambrian Earth by cosmic rays. They suggest that the detection of natural ^{244}Pu in younger minerals can illuminate this possibility. Thus an intriguing cloud of uncertainty still surrounds their remarkable discovery.

PLATE TECTONICS

Ancient Plate Motions

from our Structural Geology Correspondent

ONE of the problems facing the structural geologist is that of determining the net displacement related to crustal shortening across an orogenic fold belt; indeed, it is often difficult to determine even the orientation of displacement vectors giving the direction in which the opposing edges of the belt have moved. Most orogenic zones have their constituent fold and thrust structures developed parallel to the gross linear trend of the belt and it is this conformity that has led most structural geologists to assume that the fold belts have been developed as the result of direct orthogonal closing of the margins, rather in the fashion of the closing jaws of a vice.

The theory of plate motion makes this situation the exception rather than the rule, for only in extreme conditions will the relative motion of colliding plates have occurred perpendicular to the plate margins. W. B. Harland (*Geol. Mag.*, **108**, 27 ; 1971) has formulated a range of deformation situations which can be developed as a result of varying relationships between the direction of plate motion and the attitude of the plate edge. In this analysis the traditional regimes of extension, transcurrence and compression occur only as the result of special orthogonal relationships between moving plates.

For the general motion of plates Harland recognizes two novel regimes: transtensile regimes operating in zones of oblique extension, and transpressive regimes in zones of oblique compression. The former is typified by the opening of the Atlantic Ocean where the spreading ridge is repeatedly offset by transform faults, whilst it is the latter that is particularly pertinent to the present discussion.

During the early stages of deformation, fold and thrust structures will tend to develop perpendicular to the motion of the colliding plates and hence oblique to the plate margins. If the structures were to be frozen at this stage there would be no difficulty in recognizing both the transpressive nature of the deformation and the direction of motion of the associated plates. As the two plates continue to move, however, one plate sinks beneath the other and so these early structures are increasingly transpressed, the fold axes and thrusts being gradually rotated into alignment with the plate margins. The effects of transpression can, therefore, be divided into two distinct stages: first, a component of compression with shortening parallel to the plate motion and, second, a component of transcurrence with extension parallel to the plate margins.

The various manifestations of the extension component outlined by Harland are not by any means always easy to recognize and this factor has largely contributed to the false impression that most fold belts have been developed by orthogonal compression. Some measure of the direction of plate motion can be reached by virtue of the fact that the smaller the angle between the plate margin and the direction of plate motion the greater the component of transcurrence. But it is unlikely that even detailed strain analysis of a fold belt would lead to any precise assessment of the displacement vector, as normally the strain will be heterogeneous throughout the belt.

A. G. Smith (*Bull. Geol. Soc. Amer.*, **82**, 2039 ; 1971) has suggested a far more compelling model to determine ancient plate motion. Smith's reasoning is based first on the fact that, in recent oceans, plate motion is parallel to transform faults and perpendicular to spreading ridges and, second, on the contention that it is possible to reconstruct ancient plate margins—and hence plate motions—by restoring the past positions of fold belts, transforms and spreading axes. Clearly, the reliability of the restoration of the plate margin will decrease with age, but Smith has been able to reconstruct the relative positions of the continental areas surrounding the Mediterranean by means of a computer match of the continental margins which he showed to be consistent with a three stage model for the opening of the Atlantic.

The model demonstrated the existence by Lower Jurassic time of an extensive Tethys Ocean, entirely east of and separate from the present Mediterranean, which was gradually and completely closed during the three distinct movement phases associated with the opening Atlantic. Smith postulates that the Great and Little Caucasus Mountains represent transpressive fold belts developed by the closing of the Tethys ; the former along the northern margin with Laurasia and the latter along the southern margin with Gondwanaland. The west to east plate motions involved can be determined from the N–

Palaeozoic Movement in the Iberian Peninsula

THE geological structure of central and southern Europe is dominated by features formed during two collisions between continents. The first of these occurred before the Atlantic was formed when a land mass extending from present-day North America into northern Europe impinged on north-west Africa and an extensive mountain system formed in central and southern Europe. These movements ended about 225 million years ago and were followed about 200 million years later by a collision between Africa and southern Europe which occurred as the Atlantic opened and the Tethys Sea, which lay along the southern flank of Europe, finally closed.

Understanding the structures formed in the earlier of these collisions is particularly difficult because the Hercynian fold belts formed at that time were disrupted by the more recent movements and over much of Europe have been buried by younger deposits. In the past few years it has become clear that the most recent approach of Africa and Europe was accompanied by several subsidiary displacements as smaller blocks of crust were rotated or squeezed between the colliding continents. The rotation of Spain and Portugal, first postulated by Carey, is one instance in point. The reality of this rotation has been substantiated by palaeomagnetic measurements within the Iberian Peninsula and by evidence obtained on the floor of the Bay of Biscay which indicates that the bay developed as France and Spain separated. But it is still far from clear how the various smaller blocks, displaced during the Alpine movements, were originally situated. Analysis of contemporary earthquakes indicates the sense of movement of the smaller plates of crust at present, but earlier movements have to be inferred by other means.

An article by Ries and Shackleton in next Monday's *Nature Physical Science* bears in two ways on this problem. The article presents a new synthesis of Palaeozoic structures preserved in north-west Spain and northern Portugal. It thus provides direct evidence of the possible nature of Hercynian movements in this part of the Palaeozoic fold belt. But the structures recognized by Ries and Shackleton are so large that it seems possible that they once continued outside Spain and Portugal and so may, in the future, be used to reconstruct the relationships as they existed before later movements opened the Bay of Biscay. The structures are complex; the critical new point is the recognition by Ries and Shackleton that several isolated masses of Precambrian rock now found above younger strata once formed part of a thrust mass of crystalline rock. They suggest that this formed a plate of continental crust driven from a westerly source, presumably as a result of a Palaeozoic collision of continents. If their tentative synthesis is supported and can be extended into other parts of the Hercynian chain, the results of Ries and Shackleton may also throw light on the nature of the much younger movements which disrupted south-west Europe in Tertiary times.

S attitude of the restored Lower Jurassic spreading ridge, remnants of which are found in the ophiolite sequences of Jugoslavia and Albania, and the E–W transform between Spain and North Africa.

Powerful as this method is in unravelling the complex plate motions involved in the Alpine Orogeny, we have as yet completely inadequate data for it to be used in connexion with the older orogenic belts.

SELENOLOGY

Astronauts in Britain

by our Astronomy Correspondent

BRITAIN'S tight-knit lunar and planetary science community last week had more opportunities than usual for getting together. On Monday morning nearly two dozen lunar scientists gathered at Cambridge for a private session with the Apollo 15 astronauts, most of them later hot-footing to London for an afternoon meeting of the Royal Society discussion group on lunar and planetary sciences. On Friday many of them were back in London again, this time for a discussion on the temperature regime within the Moon, the first of this season's specialist meetings of the Royal Astronomical Society which have become such a success since their introduction last year.

Of the three meetings, that at the Royal Society was the most significant. Attended also by Mr J. Smith and Mr J. Hosie of the Natural Environment Research Council and the Science Research Council respectively, the chief sources of support for British lunar and planetary sciences, the meeting included a review of the programmes that are under way and the prospects for the future. One interpretation of the outcome of the meeting was that the research councils could offer little hope of a diversion of funds to the lunar and planetary sciences in the foreseeable future.

Earlier in the day the dialogue with the Apollo 15 astronauts uncovered no information that had not already been revealed by Houston. Nevertheless the way in which the meeting developed, with attention centring on what might be termed lunar stratigraphy, suggested that in future the factors that have resulted in the morphology of the lunar surface may soon be receiving as much attention as the petrology of the lunar samples has up to now.

Colonel David Scott and Colonel James Irwin, who made up the Apollo 15 landing party, were lucky in being the first to visit an area of the Moon having a rich landscape. But they were unable to throw any light from their personal observations on the origin of the Hadley rille, the most striking feature in the landing area. There were certainly no markings on the floor of the 400 m deep rille that indicated to the astronauts how it might have been formed. But Scott reported that the rille appeared to cut through a well-defined unit of rock—visible on the wall of the rille opposite the landing site—that appeared to contain between eight and twelve sublayers in a thickness of eight metres. Although photographs from orbit have indicated that some other rilles show fairly well-defined shelves, Hadley rille was not previously known to contain such a feature. There was some discussion at the meeting about whether the sublayers represent separate flows of lava or differentiation within a single unit.

Markings on a large scale were prominent on several of the hills around the landing site. In particular the visible face of Mount Hadley has a grid of subhorizontal striations which are crossed by another grid of more steeply dipping markings. There seems to be a possibility that one set of markings represents fracturing in the rock, this pattern interacting with erosion of the surface material of the mountain to generate the second set of markings.

Apollo 15 was of course the first of the J series of missions carrying instrumentation that is more sophisticated than was possible on the early pathfinding flights. In particular the addition of the lunar rover allowed the astronauts to cover four times the distance that was possible for the crews of Apollos 11, 12 and 14 and to collect 78 kg of samples, compared with only 98 kg from the three previous missions put together. Colonel Alfred Worden, who was responsible for the command module while his colleagues were on the lunar surface, reported that the high precision mapping cameras that were carried for the first time on Apollo 15 were used to cover about eight per cent of the front surface of the Moon. From photographs taken from orbit of the landing craft with the lunar rover parked beside it, Worden estimated the mapping camera to have a resolution of better than 1 m. No doubt the output from the mapping camera will be valuable in the choice of a landing site for Apollo 17, the last of the Apollo missions in the foreseeable future.

The experiments left behind on the surface also seem to be functioning as anticipated; in particular the seismometer at last completes the triangle of stations that the lunar seismologists need to pinpoint the epicentres of moonquakes. One source that demonstrates activity associated with the perigee of the Moon's orbit around the Earth was reported to have been located to the south of the Apollo 12 and 14 landing sites.

Colonel Irwin also reported what amounted to a road test of the rover. It reached a maximum speed of 13 km hr^{-1}, well in excess of the expected maximum of 9.3 km hr^{-1}, and in fact he and Colonel Scott were able to average 9.6 km hr^{-1}. In spite of the initial difficulty the rover had a responsive steering, and Irwin was surprised at how well it climbed slopes where the dust layer was deep enough to make walking difficult.

The meeting at the Royal Astronomical Society, which had Professor Raymond Hide as chairman, was concerned with the temperature structure of the Moon. The approach taken by several speakers was to point out the limits on the thermal history of the Moon that can be set from different types of measurement.

Variability of OJ 287

THE way in which radiation from a quasar in different parts of the electromagnetic spectrum is related to one common source—if it is related to a common source at all—remains a mystery. One of the best ways to investigate such a relation is to study fluctuations at different wavelengths in the same source; recently, BL Lac, a possible quasar, has been studied in this way. Now, H. M. Dyck and his colleagues have studied the source OJ 287 in the 0.36 to 3.4 μm range, hoping to relate their observations to those at radio frequencies and in the optical part of the spectrum. In next Monday's *Nature Physical Science* Dyck *et al.* report observations carried out in September and October 1971 in order to determine the photographic magnitudes of the source.

These observations are suggestive of a power law spectrum with index close to one, consistent with other observations of quasars but rather flatter than the spectrum of the known large amplitude variable sources. It seems that OJ 287 is bright enough in the infrared for sufficiently accurate measurements to provide useful comparison with simultaneous observations at optical and radio wavelengths. In order to be useful, such observations must, of course, be carried out simultaneously, and Dyck *et al.* plan to make further photographic observations from January 3 to 26, 1972, when they hope that other observers will cooperate in a programme of observation at different wavelengths.

PATTERN RECOGNITION

Legs and Beaks

from our Animal Behaviour Correspondent

THE problem of how animals recognize patterns of stimulation from their environments is complex and difficult, particularly where apparently similar stimuli elicit two different responses. Finding the physiological basis for such pattern recognition is of considerable interest. Electro-physiological investigations of the visual system of the cat by D. H. Hubel and T. N. Wiesel (*J. Physiol.*, **148**, 574; 1959) revealed the presence of units specifically responsive to vertical dark bars. Hubel and Wiesel subsequently found (*J. Neurophysiol.*, **28**, 229; 1965) other cells in the cortex of the cat which respond to a slit or bar, but only if it is of limited length. These they called "lower order hypercomplex" cells. Recently, J. P. Hailman has used behavioural evidence to infer that the visual system of a gull chick contains units at least as highly organized as these hypercomplex cells (*Anim. Behav.*, **19**, 328; 1971).

A newly-hatched laughing gull chick (*Larus atricilla*) will peck at its parent's down-pointing, reddish beak and this induces the parent to regurgitate food. In spite of the fact that the legs of the parent gull provide all the known relevant stimulus characteristics (size, shape, colour, orientation) that elicit the beak-pecking response, even newly hatched chicks are able to discriminate legs from beak. They only rarely peck at their parent's legs.

Hailman found that a rod or stripe held vertically in front of the chick so that it projected from above and stopped in the centre of the chick's visual field (as would a beak) would be readily pecked by a chick. A chick was much less likely to peck at a rod or stripe projecting vertically upwards from the floor and ending in the centre of the visual field (about where the legs would join the parent's body). This provided a clue as to how the chick was discriminating between leg and beak.

Hailman at first thought that the visual system of the chick contained nothing more complicated than units detecting vertical bars, that is, units which respond to the presence of vertical bars however long or short the bars might be. If more of these units were connected to the upper half of the retina than were connected to the lower half, this would explain why the "beak" stimulus was more attractive than the "leg" stimulus, as the rod pointing downwards from above would excite more of these units than the rod pointing upwards from below. But a long vertical stripe which cut across the whole of the chick's visual field ought, in these circumstances, to be an even better stimulus, as it would stimulate more of the retina than either of the half-bars.

This expectation was not confirmed. The full-stripe stimulus elicited less pecking than the downward pointing half-stripe (the "beak"). This means that there must be some cells which integrate information from different parts of the retina and respond only when there is a dark vertical bar in the upper portion of the retina and not such a bar in the lower half. They detect not just vertical bars in certain places, but their absence from other positions as well. Such an operation is similar in complexity to that performed by the cat's cortical cells described by Hubel and Wiesel. The search for the units responsible for the gull chick's perception can begin in the knowledge that the perception is organized in a fashion at least as complex as the hypercomplex units of the cat.

LIPID MEMBRANES

Nervous Hysteresis

from our Membrane Correspondent

MORE than thirty years ago the lipid bilayer was put forward by Danielli as an important structural element in biological membranes. Interest in the role of membrane lipids has since fluctuated but is currently very strong and one of the recent areas of activity concerns the role of lipid phase transitions.

In the past few years a battery of physical methods (X-ray diffraction, nuclear magnetic resonance, differential thermal analysis and the like) has been brought to bear on the subject of phase transitions in phospholipid–water systems and most of the emphasis has been on the so-called melting of the phospholipid hydrocarbon chains in lamellar lipid arrays (bilayers). Over some narrow temperature range characteristic of the particular phospholipid there is usually a transition in the configuration of the hydrocarbon chains from a relatively rigid structure, like that in solid hydrocarbons, to a much more fluid state. This fluid state presents less of a barrier to permeating molecules and ions and is thus the state in which the lipid bilayers would be expected in functioning cell membranes. This expectation was borne out in some recent work of G. B. Ashe and J. M. Steim (*Biochim. Biophys. Acta*, **233**, 810; 1971), who showed that for growth of bacteria to occur it was necessary for the membrane lipids to be in this fluid state.

Attached to their hydrocarbon tails phospholipid molecules also, of course, have hydrophilic head groups. How these head groups might behave at transition temperatures has often been only a matter of passing comment but they evidently also undergo some change in spacing and configuration. How they might do this and its implications in biological membranes is the subject of a recent report by H. Träuble (*Naturwissenschaften*, **58**, 277; 1971).

Träuble used the popular fluorescent probe 1-analino-8-naphthalene sulphonate (ANS) to investigate the model membrane system in aqueous dispersions of dipalmitoyl phosphatidyl choline (lecithin) which undergo a phase change in the temperature range 40–46° C. Träuble showed that the ANS was intercalated between the head groups at the surface of the lecithin bilayers and the increase in fluorescence which he

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Cellular Ribosomes in Arenoviruses

THERE are so many well documented examples of viruses which contain cellular enzymes and/or nucleic acids that Pedersen's claim to have detected ribosomes in lymphocytic choriomeningitis virus particles is not perhaps all that surprising. Electron micrographs of this virus and its relatives reveal within the virions sand-like or ribosome-like granules, from which the group gets its name, the arenoviruses. Pedersen, as he reports in *Nature New Biology* next Wednesday, set about characterizing the RNA species in lymphocytic choriomeningitis virus (LCM virus) in an attempt to establish that these granules are ribosomes. His results substantiate this idea.

The viral RNA is resolved by gel electrophoresis into four components, two of which co-electrophorese with the two cellular ribosomal RNAs. Viruses grown in cells exposed to low doses of actinomycin D, which inhibit ribosomal RNA synthesis, lack these two species of RNA. The two remaining species, presumably authentic LCM virus genomic RNAs, sediment in sucrose gradients at 23S and 31S and probably have molecular weights of about 1.1×10^6 and 2.1×10^6 respectively.

Because the two putative ribosomal RNAs in LCM virus particles account for about 50 per cent of the total RNA and because treatment of the intact virions with ribonuclease does not eliminate these two RNA species, Pedersen is confident that they are not simply contaminants adsorbed to the surface of the virus particles. In short, the granules seen in electron micrographs of the arenoviruses are almost certainly ribosomes which are presumably engulfed into the virions as they bud from the surface of infected cells, electron micrographs of which reveal accumulations of ribosomes at the site of progeny virus formation.

observed with temperature was attributable to the increased number of binding sites for ANS which were available at the higher temperature. Thus there was evidently a change in head-group configuration with temperature. A comparison of the enthalpy change for the head-group transition, which was calculated from the Van't Hoff equation with published values for the whole process (involving heads and tails), led to the conclusion that the transition is a cooperative process. The "cooperativity factor" (σ) was of the same order as that found for the helix-coil transition of polyglutamic acid. This large degree of cooperativity may be thought of as the nucleation of a two-dimensional "crystallization" of the head groups on cooling.

Changing the *p*H or calcium concentration was shown to alter or initiate the phase change and it was also shown that in the presence of multivalent ions and also, interestingly, of acetylcholine, the system exhibited hysteresis. Hysteresis means that a given state of a system depends on its past history and thus the system is, in a sense, capable of information storage. Such a hysteresis is also capable of giving rise to oscillatory fluxes in membranes. Träuble also used the temperature-jump method to investigate the rate of the phase change and found that the relaxation time could be markedly reduced by the presence of cholesterol in the lipid phase. With calcium in the aqueous solution as well, the relaxation time was further reduced to the order of 1 ms, which is getting down towards the duration of a nerve impulse. This effect of cholesterol implies a new role for it in biological membranes—that it enables the membrane lipids to undergo a rapid phase change.

These lipid phase changes may be important in the function of the membranes of temperature receptors. Whether such processes are of any relevance in the function of nerve cells remains at present no more than an interesting speculation.

RNA PHAGES

Progeny Release

from our Cell Biology Correspondent

WE know more about the biology of R17, Qβ and the other RNA phages—the simplest known phages—than any other group of viruses. The three genes which comprise their genome have been mapped and their functions defined, and two of the proteins specified by these genes have been sequenced. Large segments of the RNA of these viruses have been sequenced and it cannot be long before the entire sequence of the R17 or Qβ genome has been elucidated. The replicase of phage Qβ has been isolated pure and used to replicate the Qβ genome *in vitro*. Phage particles have been assembled *in vitro* from coat protein, assembly protein and RNA, and the strategy of the viral replication, the way in which ribosomes, coat protein and replicase compete for the viral RNA has been worked out. With so much already under their belts, molecular biologists might be forgiven for regarding the RNA phages as a field of research with nothing much of interest left to be discovered. While it is true that what remains to be found is perhaps unlikely to be as exciting as that found already, the results of recent work by Engelberg and Soudry (*J. Virology*, **8**, 257; 1971) and Passent and Kaesberg (*ibid.*, 286) justify their persistence with these phages.

Engelberg and Soudry have tackled the problem of the release of progeny Qβ phages from infected cells; a process which does not involve a lysozyme-like enzyme specified by the phage. At 37° C infected *E. coli* lyse, whereas at 30° C infected cells liberate progeny Qβ particles without being lysed. This nonlytic release is reminiscent of the release of the filamentous DNA male specific phages, first discovered by Hoffman *et al.* working with MS2, and suggests that the host contributes to the release mechanism. Engelberg and Soudry have now obtained direct evidence that this is the case by using chloramphenicol and rifampin to inhibit host protein and RNA synthesis, respectively. Both these drugs inhibit the release of progeny phage irrespective of the temperature at which the cells are cultured. Inhibition is not immediate but occurs within about 15 minutes at 37° C and 30 minutes at 30° C, suggesting that a labile host protein is involved. Further evidence for this conclusion comes from the finding that rifampin does not inhibit the release of Qβ from infected, mutant cells which are resistant to the drug because they contain a rifampin resistant DNA dependent RNA polymerase (DNA transcriptase). Such resistant mutants continue to make messenger RNA in the presence of rifampin, and also to release Qβ. Engelberg and Soudry reasonably conclude, therefore, that a protein specified by a host cell gene is required for continued release of this phage. Short lived protein appendages of male bacteria, the F pili, are the obvious candidates for the release protein.

Passent and Kaesberg have found that in the presence of rifampin, progeny Qβ particles are not released because, they postulate, particles are not assembled. Their experiments show that in the presence of rifampin Qβ, RNA is replicated normally, coat protein is made in almost the same amounts as in the drug's absence (as is the assembly protein) but the yield of phage particles is decreased by about 95 per cent. When resistant *E. coli* are used, the yield is unaffected by the drug. Rather than invoke some failure in a release mechanism, Passent and

Brain and Brawn

THE fine microfilaments which so abound in nerve cells and are particularly prominent near the tips of growing axons are made of actin or, to be more precise, of a protein with striking chemical similarity to muscle actin. That is the remarkable conclusion drawn by Fine and Bray from a series of elegant experiments reported in next Wednesday's *Nature New Biology*. They have isolated the two chief proteins from neurones taken from chick sympathetic ganglia and maintained in culture. These two proteins each account for about 20 per cent of the total protein and one, with a molecular weight of about 55,000, is tubulin, the subunit protein of microtubules. The second major protein, which has a molecular weight of about 45,000, co-purifies and co-electrophoreses on SDS acrylamide gels with muscle actin.

Fingerprints of this protein labelled with 35S methionine can be almost completely superimposed on fingerprints of chick breast muscle actin. The two fingerprints are not completely identical, however, and so at this stage there remains the possibility that the neurone actin is not identical to muscle actin but the two proteins cannot differ by very much, if at all.

As Fine and Bray comment, it is not perhaps particularly surprising that nerve cells contain large amounts of actin, for axons grow at rates as high as 50 μm per hour and the tip of the growing axon continually undulates and such motility presumably demands some form of contractile apparatus. They have also obtained evidence which indicates that actin or an actin like protein is in chick embryo lens, lung, skin, heart, pancreas and kidney cells. Furthermore, fingerprints of chick embryo brain actin are so similar to those of muscle actin that the two proteins may well be identical although, as Fine and Bray say, "nothing short of the total amino-acid sequences of the two proteins will establish complete identity".

It seems therefore that actin may be universal to all cells at some stage in their development, the intracellular location and precise function of the protein being in part determined by the other proteins with which it interacts.

Kaesberg postulate that rifampicin blocks the synthesis of some host factor required for the assembly of the phage. It should, of course, be possible to test this idea by examining cells infected in the presence of rifampin, either by electron microscopy or by a bioassay of homogenates, for progeny phage particles.

POLYNUCLEOTIDES

Base Behaviour

from our Molecular Biology Correspondent

In the current issue of *Biopolymers* are to be found a group of papers which look deeply into the secrets of nucleic acid structure. Of late, a dispute has centred on the nature of the simplest polynucleotide form, the unpaired unstacked chain. This was viewed, according to disposition, as a rather stiff random coil with a degree of articulation determined by the torsional angles of the backbone bonds, or as a residually stacked structure in which adjacent bases tend to oscillate in parallel planes. Felsenfeld and his colleagues examined poly A (which by optical criteria is substantially stacked) and poly U, the optical properties of which give no evidence of any interactions between bases, and showed that under ideal solution conditions (θ-point) the latter fulfils all the criteria of random coil behaviour. Poly A by contrast is much more rigid, tending to a rod-like condition at low temperature. At high temperatures, however, the structure melts, and approaches the same hydrodynamic state as poly U.

Achter and Felsenfeld (*Biopolymers*, **10**, 1625; 1971) have now driven this lesson home by a similar examination of the hydrodynamic character of apurinic acid, prepared by Chargaff's procedure of acid hydrolysis of DNA. The resulting preparation has lost about half the bases, and is therefore, one supposes, essentially devoid of interbase interactions (especially since these tend to be dominated by purines rather than pyrimidines). The frictional coefficient, as determined from the sedimentation coefficient and molecular weight of each preparation, gives, under the conditions of ideality, the unperturbed coil dimensions. The characteristic function which is normally used to describe the flexibility of the chain comes out for apurinic acid in remarkable agreement with its value for poly U, as well as poly A at 100° C. Achter and Felsenfeld now argue that, were there indeed any optically invisible interactions between bases in an apparently unstacked chain, such as poly U, then apurinic acid, in which on average three-quarters of the surviving pyrimidines are flanked by residues with no base, should have much more compact coil dimensions. This is not the case; moreover, the similarity between this deoxyribopolymer and the polyribo U seems, as an additional bonus, to destroy an earlier hypothesis—a backbone interaction involving the $2'$-hydroxyl group of ribose and the phosphate group—as a significant cause of rigidity in ribopolymers.

There appears never to have been any question but that the stacking tendency is a property of planar π-electron systems, as in the nucelotide bases or polynuclear aromatic derivatives, such as acridines and other stacking dyes. Now Formoso and Tinoco (*ibid.*, 1533) have come up with the singular observation that stacking in dimers may persist when the aromaticity of one of the partners has been destroyed—a situation rather reminiscent of the Buddhist proposition concerning the clapping of one hand. Uracil is readily reduced by a photochemical process to the saturated dihydrouracil. Reduction of this species in the dark, moreover, yields the open-chain derivative, ureidopropionic acid. Formoso and Tinoco have examined the optical properties of a series of dimers containing uridine before and after these treatments. The most striking result was for the reduced analogue of UpA, which shows considerable hypochromicity, and circular dichroism, differing in shape and sign from that of the mixture of monomers. A strange aspect is that whatever interaction causes these perturbations is not liable to thermal melting.

In the ureidopropionic acid derivative, the effect is much greater and is broken down by methanol, though again not by heating. In the dihydro-analogues of UpA and GpU, the manifestations of interaction are smaller, but nonetheless noticeable, and become more pronounced when the ring is broken. The physical and spectroscopic bases of these phenomena are as obscure as the effects are unexpected. Formoso and Tinoco do not dwell on them, but suggest that they may be of conformational importance in tRNA, where dihydrouridylic acid is found.

In the same issue Davies and Davidson (*ibid.*, 1455) have extended studies of the attachment of monomeric nucleosides to single stranded polynucleotides. The binding is cooperative, and can be presumed to include an important energetic contribution from the stacking of the monomers on the polymer. In none of the combinations that have been studied is the stoichiometry of the association anything other than 2:1 in favour of the polymer. This, Davies and Davidson find, is the case even for the interaction of monomers with copolymers, such as poly UC and poly AC.

Maurizot, Blicharski and Brahms (*ibid.*, 1429) have concerned themselves with the differences in behaviour of ribo- and deoxyribopolymers, and have studied in the first place the formation of double helices by oligomers. They find that both self-association of poly C and poly A under acid conditions, and pairing of poly A and poly U (or poly T), occur much more readily—that is at shorter chain lengths—in the deoxyribo than in the ribo series. Even trimers of dA and dT will give base-paired complexes, whereas chains of rU and rA shorter than seven residues do not associate. These stability differences must be expected to have implications for replication and transcription and the interaction of DNA and RNA with enzymes in general.

Ingredient Y

One of the interesting current problems in nucleic acid biochemistry is to find a function for the minor nucleotides present in transfer RNA. It is known that some of them are in themselves cytokinins, or growth factors in plants, but it is by no means obvious why they should appear in tRNA. One of the most unusual structures is that of the so-called Y-base, which occurs in phenylalanine tRNA. It is noteworthy for its strong fluorescence, and this property has been widely used for the estimation of distances between the anticodon loop, where the base occurs, and the chain termini, to which other fluorescent groups can be chemically attached, and also for observation of interactions of the tRNA with other molecular species. Last year the structure of the Y base from yeast tRNA was determined by a group working at Columbia University, and has a strange structure, the purine being converted to a derivative in which two amino groups in adjacent positions on the six-membered ring form part of a third aromatic ring.

In next week's *Nature New Biology*, Nakanishi *et al.* report the structures of the corresponding base from several mammalian species, which, chromatographic and other evidence suggests, are identical also with the Y base from wheat germ phenylalanine tRNA. The structure for the analogous base from beef, calf and chicken liver, established by degradation and mass spectrometry, resembles that of the yeast Y base, but contains a peroxide group in a ring-substituent chain. This is a remarkable and unexpected compound to be found in a cell. In rat liver the phenylalanine tRNA contains a mixture of the Y base, as found in yeast, and the peroxide derivative.

The Problem of Newcastle Disease

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Newcastle disease, the predominant form of fowl pest in Britain, can only be effectively controlled if improvements in vaccines and methods of administration are coupled with better farm hygiene.

THE term "fowl pest" refers to two different diseases. The first to be described was fowl plague which is a rare virus infection of chickens caused by a strain of influenza virus first recorded in Italy in 1878. This is a rapidly lethal poultry disease, characterized by high fever, cyanosis and rapid death. The disease shows little tendency to spread, however, and has seldom proved difficult to control. The second disease is Newcastle disease which is now widespread in most countries. As the two diseases are both respiratory diseases of chickens caused by viruses and give rise to symptoms which are not dissimilar, they are for legislative purposes referred to together under the heading of "fowl pest". Nearly all the cases of fowl pest which have been recorded in Britain have been caused by Newcastle disease virus with only two recorded cases of fowl plague since 1929. The 1970 epidemic was caused by a strain of Newcastle disease virus which is both more virulent and more contagious than previous isolates, and it is this virus which causes constant losses in the chicken populations in most countries; it is the one which can cause severe economic losses unless effective control measures are constantly practised.

Early Evidence

The infection causes respiratory symptoms in its milder form and in the case of the more virulent strains these are more severe and are accompanied by severe nervous involvement leading to paralysis and death. The disease was described by T. M. Doyle, a research worker in this laboratory, who investigated a series of outbreaks of a hitherto unrecognized disease among chickens in the Newcastle upon Tyne area in 1926. In the same year the disease was described by Kranveld in Batavia and after this it was reported from various countries, chiefly around the Indian Ocean and nearly always close to seaports. This suggests that the disease was spread by man. Its origin is, however, still obscure. Crawford first diagnosed the disease in Ceylon and suggested that its spread may have been associated with the transport of chilled meats that was developing in the 1920s and the discharge of the offal of poultry and of game birds which were carried in ships' stores.

One of the few initial cases that was recorded was at Rhaniket in India which is about 600 miles from the sea; after the appearance of the disease there it spread steadily across India. The effects of the disease were sufficiently dramatic for us to be sure that it had not been seen in that country before 1927, and although little is recorded of diseases of poultry in Asia before the 1920s there is nothing to suggest that it had been seen in domestic poultry before 1926. An attractive theory is that the virus had existed and still exists commensally in some species of wild birds from which it occasionally escapes into domestic poultry, causing recognizable disease. Circumstantial evidence suggests that this commensal state exists in species which inhabit South-East Asia, but it is almost certain that the reservoir does not exist in more temperate climates. The virus has been recovered from a large number of species in many parts of the world. Cases in Europe, however, almost certainly arise from cross contamination from outbreaks of disease in domestic fowls and, with the exception of pheasants, disease in non-domesticated birds seems to be very limited.

Until about 1940 outbreaks of the disease tended to be rather sporadic although in individual flocks the condition was severe. At this time the disease had not been recognized in America and it was not until 1944 that Beach showed that the relatively mild condition which had existed for several years in the United States under the name of avian pneumoencephalitis was in fact a mild form of Newcastle disease.

The milder forms of the disease were usually found in temperate climates, whereas the more virulent forms occurred in the tropics; outbreaks of intermediate virulence were evident around the Mediterranean. From time to time the more virulent forms of the disease have spread but they have tended to subside after control by vaccination and isolation or slaughter, leaving a lower level of less virulent disease. The most dangerous form of the disease is caused (as in the present outbreak) by a virus which is not of extreme virulence but which spreads too rapidly for control by slaughter because of its high contagion. It causes a heavy buildup of virus which provides a severe challenge to birds with no or little immunity. Under favourable conditions the spread of such a virus from one set of premises to another can be very rapid.

During and after the Second World War the disease continued to spread from country to country and the total incidence rose steadily. In the early stages when poultry flocks were fairly small and more self-contained, many of these cases were self-limiting. As the poultry industry grew in size and intensity, however, the spread of the disease became more rapid until in areas of intensive poultry keeping it became endemic.

By this time vaccines to control the disease had been developed. The first was produced from a virulent form of the virus isolated in Hertfordshire in 1933 and was developed by Iyer, a visiting Indian worker who—in conjunction with Dobson—successfully attenuated the virus by repeated passage in fertile hen eggs. On his return to India, Iyer and his colleague Idani set about repeating the work with a local Indian strain and produced the very successful if somewhat virulent vaccine called the Mukteswar strain, which is now used all over South-East Asia. This strain was also used by Simmins during the war in Palestine, and, although effective, was considered to have too much residual pathogenicity. This stimulated the development of another strain which is slightly safer and has been named after the originator as the Haifa-Komarov strain. Vaccine from this strain is now used widely throughout Africa and the Middle East and in Russia.

These strains all possess considerable residual virulence and are not suitable for areas where the effects of the disease are more mild and where competition rules out the use of agents which might cause reactions severe enough to affect production. In the United States, where less pathogenic

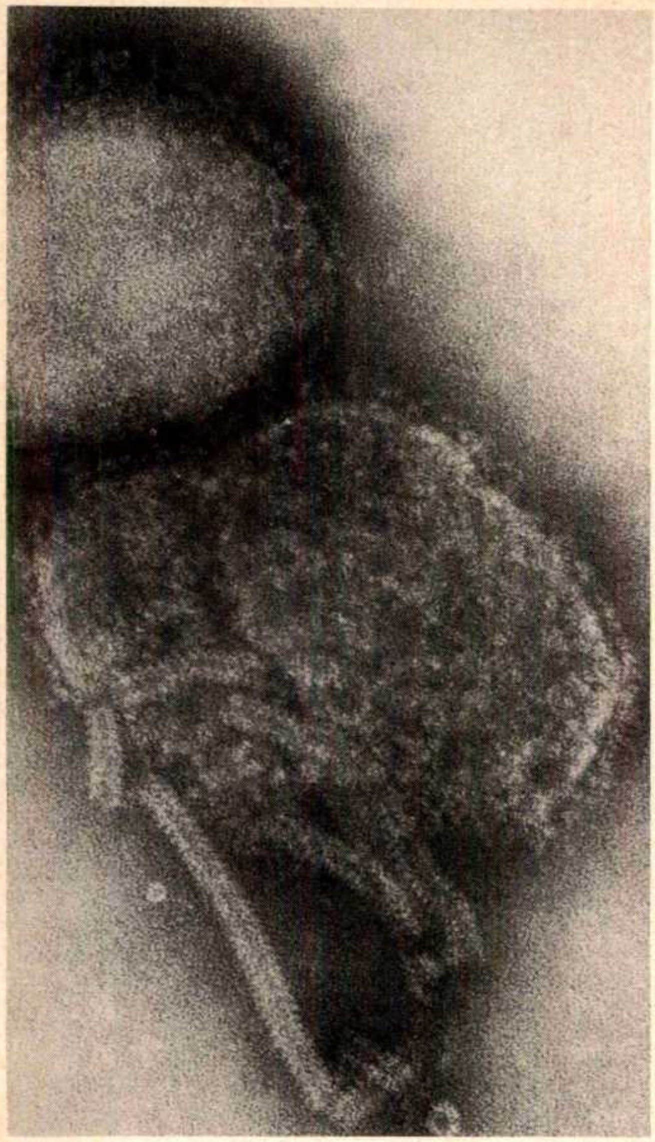

Fig. 1 Two Newcastle disease virus particles. The upper one is intact whereas the lower one is broken and the helical internal component is visible. This internal component is the ribonucleoprotein of the virus and the membrane is the virally altered cell membrane component. (×250,000.) This micrograph was kindly supplied by Dr June D. Almeida, Royal Postgraduate Medical School, DuCane Road, London W12.

strains existed naturally, Hitchner selected one which was naturally avirulent and tested it as a possible vaccine. This strain—the B1—has become the most widely used vaccinal strain in the world and has been followed by several others all characterized by their intrinsically low virulence combined with a residual ability to invade the chicken's respiratory tract,

By 1950 the disease had become the largest potential cause of loss to the chicken farmer, and a variety of control measures had come into force. Where the incidence of a virulent virus made disease recognition straightforward and where the incidence of the disease was low, control by slaughter was adopted. In Asia control was by vaccination, usually with a mild virus of the B1 type at first and then by the individual application of the Mukteswar strain. In the United States, the somewhat lower virulence of the naturally occurring field virus allowed less rigorous control measures to be adopted and the mass application of the B1 and related LaSota strains has been the most widely adopted method of control.

But these mild or attenuated live virus vaccines can still induce a small amount of respiratory disease which can in some instances be complicated by secondary infections, so their use does not constitute an ideal form of control. When Britain ceased to use compulsory slaughter of infected flocks it was decided to use an inactivated vaccine which had recently been developed to a high standard. Its use brought the 1962 outbreak under control by stages, although the incidence of disease did not fall rapidly until vaccination was coupled with an increased standard of hygiene. When this was achieved the incidence of disease decreased year by year until in the summer of 1969 only one case a month was reported.

Vaccine controls the disease by reducing the death rate, and also by drastically reducing the number of infected particles shed. Poultry rearing is a very competitive industry and, inevitably, the use of vaccine became less extensive as the incidence of the disease was reduced. The number of completely susceptible birds then increased, and it was clear that a disease vacuum was being created; members both of the poultry industry and of the veterinary profession urged that a high level of vaccination should continue.

By the middle of 1970, less than half the national flock was receiving vaccine and when the disease erupted in Essex the initial spread was very rapid, partly because of the infection of a large number of susceptible birds in an area where the poultry industry is particularly dense, and partly because of the large quantities of virulent virus released by each of them.

In the present epidemic, the losses are not only due to the inherent virulence of the virus, but also to the unusually high buildup of infective virus which occurs because this strain is unusually active in the respiratory tract, and is released from infected birds in much larger amounts than strains which have a more fixed neurotropic activity.

It is not uncommon to consider disease control simply in terms of the application of sufficient vaccine to immunize the population. In the case of Newcastle disease—as with other infectious conditions—several factors complicate the issue. These include the buildup of virus in large poultry houses, thus placing neighbouring flocks in jeopardy because of the possibility of spread of the virus by wind and the likelihood of mechanical transfer from one site to another. If poultry houses are saturated, the virus buildup also increases the chance of virus carrying over from one crop to another unless disinfection between batches is meticulously carried out.

Of equal importance is the problem of unusually high levels of antibody in the breeding flocks which develop as a result of disease. These are transferred passively to the young chick through the yolk sac, and can neutralize the effect of vaccination for a variable length of time. This means that some birds can be successfully immunized soon after hatching but others are refractory until they are more than 6 weeks old. When chicks such as these are placed in contaminated surroundings, they cannot be protected by immediate vaccination, and are liable to develop the disease as soon as their maternally derived protection wears off.

Mass Vaccination

In an effort to minimize the losses that can occur in this way it is now common practice to immunize large groups of broiler chickens several times early in life in an attempt to obtain a satisfactory immune response in as many as possible at the earliest possible age. Application of vaccine to 100,000 or more birds on one site makes individual handling almost impossible, and mass vaccination methods (mixing the vaccinal virus in the drinking water or applying a fine spray of virus into the chicken house) are usually employed. The technique adopted in the last of these methods is fairly critical as too small a droplet size will cause deep penetration of virus into the lungs or air sacs where it can set up a severe reaction. In smaller flocks, such as breeder replacements, the most satisfactory way of achieving a useful and even immune response is by individual administration of a drop of vaccine into the conjunctival sac from which it travels by way of the naso-lachrymal duct to the upper respiratory tract, thus multiplying and inducing the immune response.

In the case of influenza vaccines, the choice of the correct antigenic type of vaccinal virus is all-important. Newcastle disease virus, on the other hand, belongs to the paramyxovirus group which includes the viruses of mumps, measles, rinderpest and distemper; these viruses are each antigenically homologous and therefore the problem of plurality of antigenic types does not arise. The apparent failure of vaccines for Newcastle disease has led many workers to suggest that some antigenic variation might exist and until recently the problem had not been satisfactorily solved. In an attempt to settle the question a number of research workers have worked jointly on a programme of analysis of a variety of strains of virus drawn from different parts of the world. Pennington carried out a series of cross-neutralization tests which showed that although homologous virus serum mixtures were neutralized at a faster rate than similar heterologous mixtures, there was no distinct variation between strains which might create the need for vaccines of more than one antigenic type. Similar studies were carried out by myself, Kendal, Reeve and Alexander which included a comparison of the enzyme neuraminidase from fourteen different strains. Although there was considerable variation in the growth kinetics of different strains and their ability to form plaques, there was no measurable serological variation between any of the isolates examined. The efficacy of vaccines therefore probably depends more on their quality and the efficiency with which they are administered than on any antigenic variation. It would indeed be unlikely for any member of this group of viruses to show such variation.

The efficiency of a live virus vaccine depends on its invasiveness and its power to multiply sufficiently within the chicken to set up an adequate immune response. As the invasiveness of a strain is directly related to its level of virulence, the more efficient immunizing strains are also those which will induce the most severe reactions. It was this consideration which led Britain to adopt a policy of vaccination limited to inactivated vaccines which can now be produced with high potency. Such vaccination proved very effective and it was the reluctance of the poultry industry to spend the time and money on techniques of individual inoculation which led to its eventual failure.

The addition of live virus vaccines to the drinking water is simple and cheap but the method is not very effective because the site at which the virus multiplies is the respiratory tract. It is believed that only that virus which splashes onto the nostrils and comes in contact with the respiratory tissues around the pharynx can multiply successfully. Virus which reaches the proventriculus is rapidly destroyed. The optimal dose of virus is between 10^6 and 10^7 infective particles and it is important that as much as possible of this dose reaches the respiratory mucosa of the bird. Although these vaccinal viruses are contagious, their spread is limited and the immune response that takes place is a direct function of the amount of virus introduced.

An effective response is dependent on the presence in the bird of the equivalent of about $10^{9.5}$ infective particles. To achieve this, live virus vaccines which come into contact with the bird in concentrations less than one five-hundredth of this amount must successfully invade the bird and multiply sufficiently to provide an adequate stimulus. When the bird is in the fully susceptible state this potential can be achieved, but when circulating antibody—which may be either actively or passively acquired—is present it may inhibit the multiplication of the vaccine. This makes the timing of repeat doses of vaccine particularly difficult as the chicken must be susceptible to infection before a satisfactory reinfection can take place. When there are large quantities of field virus the chance of field infection is high. The mild live virus vaccines do not multiply very efficiently when used as boosters of existing immune levels and so the secondary response that they induce is seldom very much higher that the primary response. This may be overcome by using the more invasive live virus vaccines for repeat vaccination or injecting the inactivated vaccine which is combined with a mineral adjuvant and induces a very satisfactory secondary response.

Other recent work has involved studies into the immunosuppressive nature of another poultry virus infection. My colleague, J. T. Faragher, has shown that infection early in life with the infectious bursal agent, which is thought to be a reovirus, can cause a significant depression of antibody levels to subsequent Newcastle disease vaccines. Continuing work will be designed to assess the importance of this infection as a complicating feature of Newcastle disease control.

Improving Control

Improvements in vaccines, their administration and farm hygiene are essential if more effective control over the disease is to be achieved. The live contagious vaccines of the B1 type produced in egg embryos are unlikely to be further developed although increasingly more stringent government requirements for their safety and potency now ensure that all vaccines which are available are close to their optimal level. Live vaccines produced in tissue culture systems have been available in other countries for several years. They are considered to be effective, but as they require to be injected they are more than usually susceptible to neutralization by existing immune levels. Inactivated vaccines depend for their potency on the amount of viral protein that they contain, and although tissue culture methods of production simplify the production processes it is doubtful whether they can match the virus yields obtainable in embryonated eggs. Slow growing strains multiply to a higher level than those which cause rapid death of embryos and by using these it is now possible to produce inactivated vaccines of considerable potency. Their cost and the cost of injecting birds individually means that their use will probably be confined to breeder and replacement flocks.

Programmes of administration pose additional problems. In an effort to find a compromise between the easy but relatively inefficient method of applying vaccine in the drinking water and the effective but laborious method of individual application by the ocular route, there is increasing interest in the application of the virus by spray; this is in spite of the serious side effects which can occur if the conditions of application are wrong or if the flock is predisposed to respiratory disease.

Vaccination alone cannot provide the answer. The emergence of Newcastle disease as a world problem has been closely linked to the gradual intensification of the poultry industry, and an effective programme of vaccination must be coupled with standards of hygiene that help to limit the spread of virus and, in particular, to eliminate the infection from a site following disease. The difficulty of doing this increases with the size of the units concerned, and it is known that the amount of infective virus that can be shed as windborne infection from a severely infected and sizable unit can be as much as $10^{9.0}$ infective particles per hour. Although windborne infection can play a large part in the spread of disease from severe outbreaks, the persistence of disease in an area is related to a greater extent to group practices involving rapid restocking after an outbreak of disease and the failure to segregate one production unit from another. The problems of intensification will become greater as the production of poultry increases and, to prevent a recurrence of the epidemic, continued vaccination must be coupled with improved hygiene even if this leads to increased costs.

Detection of Plutonium-244 in Nature

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Mass spectrometric measurements of plutonium isolated from Precambrian bastnasite confirm the presence of ^{244}Pu in nature. Although the existence of ^{244}Pu as an extinct radioactivity has been postulated to explain the xenon isotope ratios observed in meteorites, this is the first indication of its present existence in nature.

THE agreement between recent measurements of the Xe isotopic ratios from spontaneous fission of ^{244}Pu by Alexander *et al.*[1] with the corresponding ratios found in achondritic meteorites strongly supports the existence[2] of ^{244}Pu in the early solar system. But attempts to detect residual ^{244}Pu in nature have previously been unsuccessful, and the most recent investigation reported by Fields *et al.*[3] resulted only in an upper limit of 3×10^{-22} g/g for the average terrestrial abundance of ^{244}Pu. This limit is still well above the upper limit for the present average terrestrial abundance of 3×10^{-25} g/g which can be calculated by assuming that 4.7×10^9 yr ago, the abundance of ^{244}Pu (half-life $= 8.28 \times 10^7$ yr[4]) was equal to the present average terrestrial abundance[5] (4.4×10^{-8} g/g) of ^{232}Th, the ultimate decay product of ^{244}Pu. Because even the most sensitive mass spectrometric measurements require $\approx 10^7$ atoms ($\approx 4 \times 10^{-15}$ g) of Pu for positive detection, it is necessary to process very large samples of ores which are highly enriched in Pu.

We describe here the isolation of the Pu fraction and the subsequent detection of 2×10^7 atoms (8×10^{-15} g) of ^{244}Pu from about 85 kg of ore containing bastnasite, a rare earth fluocarbonate mineral. We also discuss the implications of the presence of ^{244}Pu in nature in the establishment of the last time of formation of the heavy elements prior to the formation of the solar system, and consider the possibility that ^{244}Pu may occur as a result of accretion from a steady state cosmic ray source.

Source of Bastnasite

Our starting material consisted of about 9 l. of 25% di-2-ethylhexylorthophosphoric acid (HDEHP) in kerosene, and was provided by the Molybdenum Corporation of America from an inventory of extractant used to purify Ce derived from a bastnasite deposit mined at Mountain Pass, California. Our sample represented the processing of about 10.5 kg of pure CeO_2 which is equivalent to 26 kg of bastnasite, or 260 kg of "as-mined" ore. This ore typically contains about 10% bastnasite together with 50% calcite, 25% barite, and 15% silica, strontianite, chlorite, monazite, galena and so on. Hot-froth flotation, acid leaching, and calcining are used to prepare a rare earth concentrate which is then roasted to convert any Ce(III) to Ce(IV). It seems probable that any Pu in the bastnasite would be concentrated in the rare earth fraction and would be present as Pu(IV), regardless of its initial oxidation state, because Pu(III) is more readily oxidized than Ce(III). After removal of the trivalent rare earths by dissolution in dilute HCl, the CeO_2 is dissolved and finally purified by extraction into HDEHP and back extraction with dilute HCl containing H_2O_2. Because Pu will extract into HDEHP but will not back extract under these conditions[6], any Pu present in the bastnasite should accumulate in the HDEHP as it is recycled.

Isolation of Plutonium

The HDEHP sample was divided into three approximately equal fractions which were processed separately. ^{236}Pu and ^{242}Pu were used to determine the amount of ^{244}Pu in each fraction. Known amounts were extracted into the HDEHP from 3 N HCl containing $NaNO_2$ to ensure that the Pu was present in the (IV) state. The aqueous phase from this extraction was checked to make certain that at least 99% of the tracers had extracted. The HDEHP was then washed with 10 to 15 l. of 6 N and 3 N HCl in 500 ml. portions to remove macroscopic impurities such as Fe or Ce. When no more mass could be detected in the washes by hydroxide precipitation, the Pu was back extracted by an adaptation of our procedure for separating Pu from large volumes of solution[6]. One litre of 2,5-di-tertiary butylhydroquinone was added directly to the HDEHP to reduce Pu to the (III) state and complex it. It was then back extracted twice by treatment with 2 l. of 6 N HCl. The combined back extractants were washed with kerosene and then evaporated to dryness under vacuum. Although very little Th should back extract in these conditions, the mass spectrometric analysis of fraction I indicated interference from Th. In subsequent analyses, the Pu was adsorbed on 7 mm internal diameter × 10.5 cm long anion resin columns and eluted with an HI-HCl mixture according to a standard Pu procedure (page 91, ref. 6). No interference from Th was encountered after this step was added. The Pu fraction eluted from this column was further processed just prior to isotopic analysis by extraction into 0.2 M thenoyltrifluoracetone and back extraction with 8 N HNO_3. We have found this necessary to reduce solids and other interferences which lower the efficiency of plutonium ion emission in the mass spectrometer.

The ^{236}Pu and ^{242}Pu tracers, complete process blanks, and appropriate volumes of new batches of reagents were analysed for ^{244}Pu. None of these showed ^{244}Pu. Our chemical yield for complete processing of Pu from HDEHP was >95%.

Mass Spectrometric Measurements

The thermal ionization plutonium isotopic measurements were all obtained utilizing rhenium V-type filaments[7] in the KAPL three stage[8] mass spectrometer in the pulse counting mode[9]. The first Pu fraction from the bastnasite contained too much Th for analysis. Although Th was eliminated from the second fraction, the sample still did not yield a sufficient number of ions of ^{242}Pu tracer to permit a good analysis, but the upper limit of 5×10^7 atoms of ^{244}Pu found is not inconsistent with the actual amount of ^{244}Pu found in the third fraction.

^{244}Pu was found in the third fraction of the bastnasite ore and was confirmed by mass spectrometry in two separate aliquots of this third fraction. The first aliquot gave a value for $^{242}Pu/^{244}Pu$ of 284±40 while the second aliquot gave a value of 266±40. The $^{244}Pu/^{242}Pu$ ratio was observed to be constant over the normal range of filament temperature (specifically, eight temperature increments). This temperature range was consistent with our experience in plutonium ion emission. Table 1 shows the mass spectrometric results obtained from the third fraction of the bastnasite. A total of 268 ions were detected at the ^{244}Pu mass position of which 26 are ascribed to instrument noise.

Table 1 Mass Spectrometric Determination of Isotopic Abundances in Plutonium Fraction III from Bastnasite

Pu mass No.	Atoms ($\times 10^{-7}$)
236	280
238	<10
239	280
240	≈18
242	565 (tracer)
243	<0.2
244	2.0

During the course of this work, mass spectrometric analyses of tracers, reagent blanks, and process blanks have been performed. None of these showed ^{244}Pu. Of the tracers used, ^{236}Pu gave the highest upper limit, $<1.7 \times 10^5$ atoms, for ^{244}Pu. Of the six process and reagent blank analyses, two gave upper limits of <4.6 and $<5.5 \times 10^6$ atoms for ^{244}Pu while all the other analyses gave limits of $<1.5 \times 10^6$ atoms. Our experience has shown that chemically pure tracers give an order of magnitude better ion emission than an equivalent amount of Pu which has undergone extensive processing before being introduced into the mass spectrometer. The higher limits observed for the process and reagent blanks than for the tracers reflect this reduction in sensitivity, which is attributed not to low chemical yields but to the influence of some unknown and uncontrolled trace impurity which inhibits plutonium ion emission. This observation is entirely consistent with our experience with the large number of trace Pu analyses conducted during the past 15 yr.

Two process mock-up analyses (without HDEHP) were also made in which 1.75×10^6 and 1.75×10^7 atoms of ^{244}Pu, respectively, were introduced along with the ^{242}Pu tracer. The mass spectrometric analyses indicated 2.02×10^6 and 1.95×10^7 atoms, respectively.

The absolute amount of ^{244}Pu detected in the third fraction of the bastnasite sample was 2.0×10^7 atoms, calculated from the $^{242}Pu/^{244}Pu$ measured ratio and the known amount (5.65×10^9 atoms) of ^{242}Pu tracer added. In addition, the measured amount of ^{236}Pu (Table 1) agreed with the 2.88×10^9 atoms of ^{236}Pu tracer added. The only correction made to the observed data was for instrument noise. Correction for possible ^{244}Pu contributions by the tracers and process blanks was not made since the data available for this were "upper limit" observations. These "upper limits" amounted to between 15% and 20% of the ^{244}Pu actually found in the bastnasite. We elect not to make an empirical correction of this type because of the data resulting from our mock-up samples. For example, in the 1.75×10^6 atoms of ^{244}Pu mock-up, we measured 2.02×10^6 atoms. This excess of 0.3×10^6 is less than 2% of the ^{244}Pu found in fraction III. Similarly, in the mock-up sample containing 1.75×10^7 atoms of ^{244}Pu, we measured 1.95×10^7 atoms. This excess of 0.2×10^7 atoms does amount to approximately 10% of the ^{244}Pu found, but could as well be caused by the imprecision of the measurement at this level. Imprecision of measurement is, of course, included in our results for the third fraction of the bastnasite.

In summary, 2.0×10^7 atoms of ^{244}Pu were found in the sample. In assigning an error to this value we include ±10% for precision of the measurement, ±5% for uncertainty in the background correction, and a possible 20% positive bias when one considers the upper limits derived from the blank runs. Thus the best estimate becomes $2.0^{+0.3}_{-0.7} \times 10^7$ atoms of ^{244}Pu per 8.5 kg of bastnasite, or 1.0×10^{-18} g ^{244}Pu/g.

The $^{239}Pu/^{244}Pu$ ratio was found to be 140 for fraction III. This low value rules out any possibility of the ^{244}Pu being due to atmospheric fallout from world-wide debris, from Nevada underground heavy element producing devices, or from highly burned reactor fuel. There is, of course, the highly remote possibility that a submicron particle of pure ^{244}Pu could somehow have been incorporated into our sample. However, ^{244}Pu had never been handled previously in the new laboratory at LASL where the processing was done, and clean room techniques were used during the course of the work.

Implications of ^{244}Pu in Nature

The bastnasite from which our sample was derived is reported to be a Precambrian deposit. The CeO_2 in the pure bastnasite is typically 30% to 50%, indicating an enrichment of the order of 5×10^5 over its average terrestrial abundance[10] of 9×10^{-7} g/g, or about 10^4 over its abundance in the Earth's crust. If one takes Podosek's[11] value of 0.013 for the ratio of ^{244}Pu to ^{238}U at the time of meteorite formation 4.56×10^9 yr ago, the present abundance of ^{244}Pu is 7×10^{-27} g/g based on an average terrestrial value[5] of 1.1×10^{-8} g/g for ^{238}U. Our single result for bastnasite indicates 10^{-18} g/g which would require an enrichment of about 1.4×10^8 for ^{244}Pu, or about 2.8×10^2 relative to Ce. On the other hand, if the ratio of ^{244}Pu to ^{238}U is as high as 0.5, a possibility indicated by Fleischer *et al.*[12], the present abundance of ^{244}Pu is 2.8×10^{-25} g/g which requires an overall enrichment for ^{244}Pu of 3.0×10^6 or only about 6 relative to Ce. The bastnasite is believed to vary widely in both Th and U content so variations in ^{244}Pu content may be expected. If, however, the detection of ^{244}Pu is substantiated at something like 10^{-18} g/g in other samples of bastnasite, it would tend to support the hypothesis that *r*-process nucleosynthesis was occurring at the time of formation of our solar system, since unreasonably large enrichment factors (for example, $>10^{12}$ for 6×10^9 yr) would be required if the last synthesis occurred much longer than 5×10^9 yr ago.

The possibility of ^{244}Pu resulting from a steady state cosmic ray source must also be considered. Dr George Bell of the Los Alamos Scientific Laboratory has pointed out to us that the present abundance of ^{244}Pu due to the influx of ^{244}Pu nuclei in cosmic rays may be comparable with, or greater than, that surviving from primordial Earth material. If the steady state upper limit incident flux of ^{244}Pu nuclei is assumed[12] to be 10^{-11} cm^{-2} s^{-1}, if the probability that an incident nucleus is stopped without undergoing disintegration is 0.1, and if, in a length of time of the order of a ^{244}Pu half-life as much as 10 km of the Earth's crust may be involved in the distribution of ^{244}Pu, the concentration of ^{244}Pu would be

$$\frac{(10^{-11}\ ^{244}\mathrm{Pu\ atoms\ cm^{-2}\ s^{-1}})(0.1)(4\times10^{15}\ \mathrm{s})}{(2.5\times10^{21}\ \mathrm{atoms}\ ^{244}\mathrm{Pu/g})(3\times10^{6}\ \mathrm{g\ cm^{-2}})}=\approx5\times10^{-25}\ \mathrm{g/g}$$

This value is comparable with the upper limit for ^{244}Pu derived from ^{232}Th, and higher than the values calculated from the ^{244}Pu to ^{238}U ratios obtained from meteorites. If this bastnasite is $>5.5\times10^{8}$ yr old, the plutonium must have been incorporated in the mineral that long ago with no further enrichment possible. The decay factor for ^{244}Pu during this time would be about 100, reducing the concentration to about 5×10^{-27} g/g, thus requiring an enrichment factor of about 2×10^{8} to give the 10^{-18} g/g reported here.

It is obviously important to confirm the present single result on larger samples of the same ore. Extension of the measurement to minerals whose age is much less than the half-life of ^{244}Pu might help in deciding whether the ^{244}Pu is primordial or originates from a cosmic ray flux. In the latter case, concentrations of ^{244}Pu up to 100 times as large might be expected since very little decay would have occurred since enrichment, that is, formation of the mineral. In fact, if reliable measurements of different age samples of a given mineral could be made, it might be possible to infer something about the magnitude of the cosmic ray flux. Measurements of other minerals, such as gadolinite, in which U, Th, and the rare earths have nearly the same enrichment factors would also be valuable since the enrichment factor for Pu might be expected to be similar. Then, if a much higher enrichment for Pu were observed, a cosmic ray origin might be indicated.

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Simplicity of Mammalian Regulatory Systems inferred by Single Gene Determination of Sex Phenotypes

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Dr Ohno predicts that mammalian regulatory systems will turn out to be less complex than is generally anticipated.

It has often been stated that compared with the *lac* operon system of *E. coli*[1] and other regulatory systems of prokaryotes, genetic regulatory systems in mammals must be enormously complicated, defying meaningful analysis at present. I suggest that this is as unsound as the notion that, since the mammalian genome contains 750 times more DNA than that of *E. coli*, the genome of which seems to contain about 4×10^{3} genes, mammalian genomes must specify 3×10^{6} different gene products.

All gene loci are affected by mutations, and mutation in a gene often contributing to the wellbeing of an organism would be detrimental. For example, mutational deficiency of individual lysosomal enzymes causes eleven different lysosomal diseases in man, many of them extremely severe[2]. As the spontaneous deleterious mutation rate per locus per organism generation is of the order of 10^{-5}, an organism with 3×10^{6} genes would be exterminated by the excessive mutation load (the overall deleterious mutation rate per generation becomes thirty). Kimura[3] estimated that if all the mammalian genomic DNA are functional genes, in order to maintain a stable population size, each mated pair would have to produce 10^{78} zygotes to assure that a few of them would survive. Because of what Haldane[4] termed "the cost of natural selection", Muller[5] as well as Crow and Kimura[6] concluded that the human genome must contain only 4×10^{4} or so genes. This number of genes accounts for only a fraction of the total DNA in the human genome. The concept that most of our genomic DNA is noninformational seems to be accepted by an increasing number of investigators[7].

When one realizes that the mutation load imposes a finite upper limit to the number of gene loci which an organism can afford to have, it becomes clear that, during evolution from unicellular prokaryotes to multicellular eukaryotes of increasing complexity, the necessary increase in number of regulatory systems had to be compensated by simplifying each regulatory system. I contend, therefore, that the direction of natural selection has been to reduce the number of components in each regulatory system as multicellular organisms attained higher degrees of complexity.

In mammals, the dosage compensation for most, if not all, *X*-linked genes is accomplished in one step by inactivation of one or the other *X* in the female[8]. It would not be surprising if a single gene locus controls this inactivation process involving hundreds of structural genes. The beauty of this mechanism is in its simplicity.

In the inducible regulatory system of mammals, hormones rather than substrates, or derivatives of substrates, serve as inducers. Accordingly, in addition to the components of regulatory systems in target cells, the genes concerned with synthesis and release of hormones in endocrine cells contribute to the mutation load. The observation that the actions of a multitude of peptide hormones are mediated through a small variety of intracellular inducers such as cyclic AMP[9] supports the view that natural selection favoured economy and simplicity in mammalian regulatory systems.

Selective pressure for simplicity must have been especially strong for the genetic regulatory system concerned with sexual development, for a mutation which results in sterility is lethal: those which do not reproduce are genetically dead. I will develop the thesis that a single gene product specified by the *X*-linked locus controls the expression of male and female phenotypes in mammals. The minimal requirement for sex determination is a set of two regulatory genes: one to mediate the developmental direction of indifferent gonads toward either testes or ovaries and the other to regulate the manifestation of secondary sex characteristics. I am concerned here only with the second regulatory system, and, for this system, the testis or the ovary merely serves as the supplier of an inducer (steroid hormone).

Sex Phenotypes

In a series of embryological experiments on rabbits and rats, Alfred Jost[10] has shown that the expression of the male or female phenotype strictly depends on the presence or absence of testosterone (an inducer) (Fig. 1). If *XY* embryos are castrated early enough, the Müllerian ducts automatically differentiate to Fallopian tubule and uterus, while the Wolffian ducts retrogress. Accordingly, an embryo acquires the female phenotype. The administration of testosterone to castrated *XY* or *XX* embryos sustains the development of Wolffian ducts toward ductus deferens, epididymis and seminal vesicles and directs the differentiation of the urogenital sinus toward prostates and penis formation. Externally administered testosterone, however, fails to destroy Müllerian ducts and these castrated embryos have the hermaphroditic phenotype. On this basis, Jost reasoned that the destruction of Müllerian ducts requires the presence of another male hormone (factor "*X*") secreted by embryonic testes.

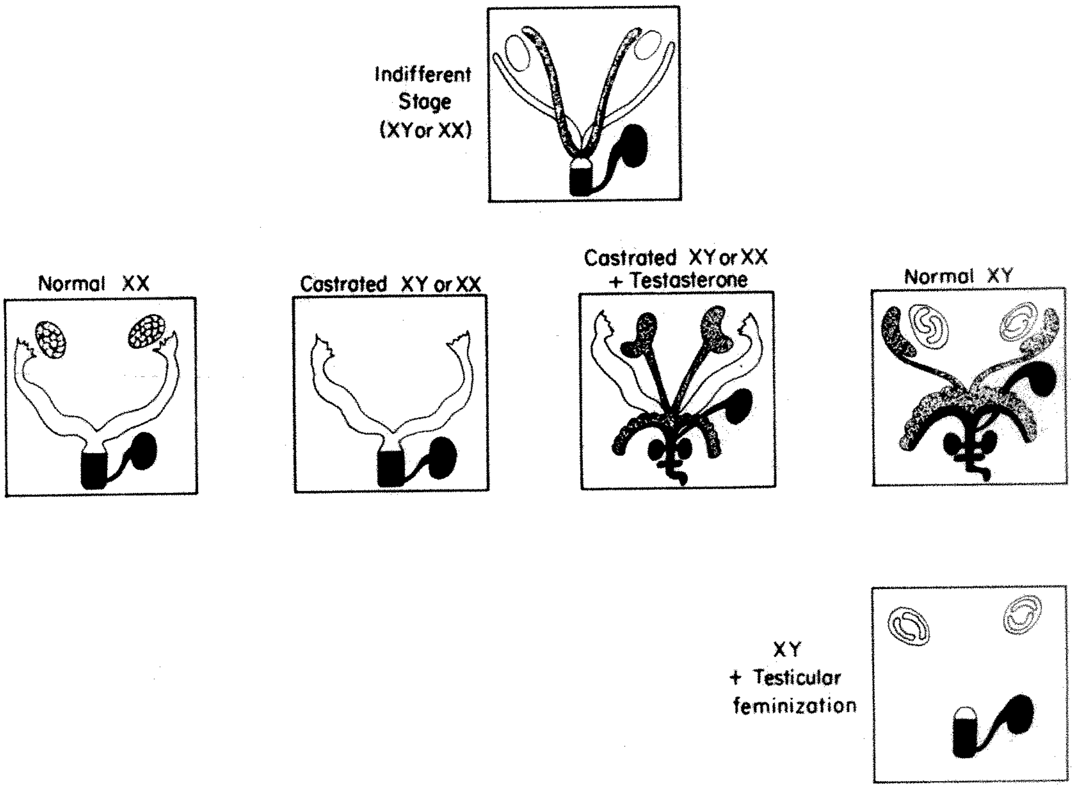
Indifferent Stage (XY or XX)
Normal XX
Castrated XY or XX
Castrated XY or XX + Testosterone
Normal XY
XY + Testicular feminization

Fig. 1 A scheme (modelled after Neumann *et al.*[32]) showing the role of testosterone and the effect of the *Tfm* mutation on the embryonic development of the Wolffian duct (shaded), Müllerian duct (outlined) and urogenital sinus (solid black). The pair of bean-shaped bodies at the top of each square signify gonads: indifferent gonad (outlined), ovary (filled with small circles) and testes (containing two tubules).

Jost's experiments completed the demonstration that maleness and femaleness can represent an induced state and a noninduced state of one and the same regulatory system. The regulatory gene product of this system must have a binding affinity to testosterone or its metabolites, or both.

Testicular Feminization

If this regulatory gene product loses binding affinity by mutation, testosterone would become totally ineffective. Such a mutation would not affect the development of *XX* females, but the *XY* male should show externally a female phenotype in spite of the presence of testes. Factor "X" secreted by testes would destroy the Müllerian duct and the Wolffian ducts not responding to testosterone would also disappear. The urogenital sinus remaining unmodified would form the vagina which ends as a blind sac (Fig. 1). This phenotype is, of course, that of the well known inherited testicular feminization syndrome originally described in man[11,12], and subsequently found in cattle[13], rats[14] and mice[15].

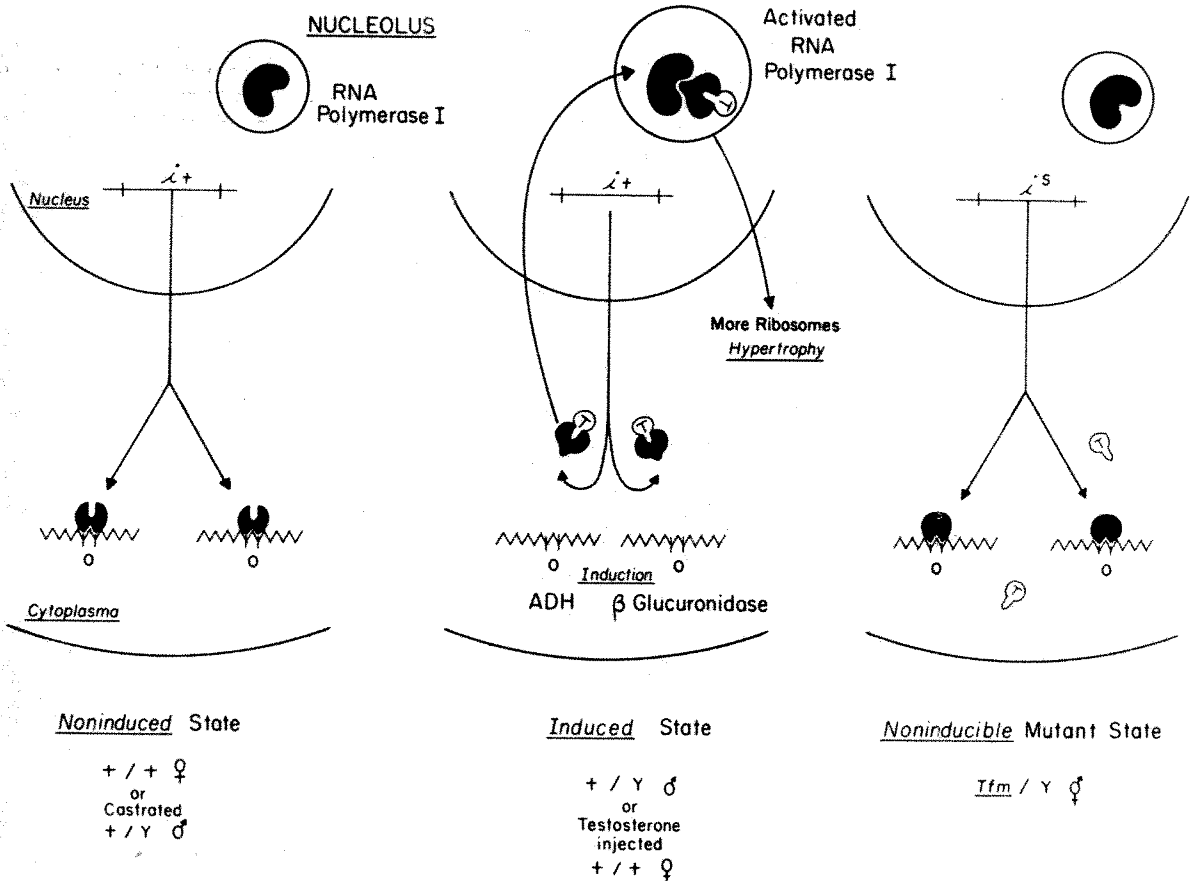

Fig. 2 A scheme illustrating single gene control of mammalian sexual phenotypes. i^+ represents the wild type allele of the *X*-linked *Tfm* locus. Its product (●) serves as a translational repressor of alcohol dehydrogenase (ADH) and β-glucuronidase in the cytoplasm until the arrival of testosterone (⚲). When it becomes bound to testosterone or its metabolites (such as DHT), it moves into the nucleus and activates RNA polymerase I in the nucleolar region, thus causing increased production of ribosomes and hypertrophy. i^s represents a mutant *Tfm* allele; its product (●) has lost the binding affinity to testosterone. The *o* (operator) region in each RNA (wavy line) signifies a homologous base sequence shared by ADH and β-glucuronidase mRNAs which is recognized by the product of *i* gene.

One point must now be clarified. Although testicular testosterone synthesis by affected males of man[16], rats[17], and mice is abnormal due to relative deficiency of either 3β-hydroxysteroid dehydrogenase[16] or 17β-hydroxysteroid dehydrogenase[17], the paucity of an inducer (testosterone) cannot be the cause of the testicular feminization syndrome. Affected *XY* surely produce more testosterone than normal females, yet normal females respond to administered testosterone exactly as do normal males, while affected *XY* do not respond at all. The testis is one of the principal target organs of testosterone; thus, testicular insufficiency is merely a consequence of this mutation.

In man, cattle and rats, the mode of inheritance has been compatible with either *X*-linked mutation or autosomal dominant mutation. Only in the case of mice has it been clearly established that this mutation resides on the *X* chromosome. Lyon and Hawkes[15] were able to show the very close linkage between this *Tfm* locus and two well known *X*-linked coat marker genes of the mouse; tabby (*Ta*) and blotchy (*Blo*). As a gene which is *X*-linked in one mammalian species is almost always *X*-linked in other species[18], we infer that the *Tfm* locus resides on the *X* chromosome of all mammalian species.

In mice, *Tfm* behaves as a point mutation and, in man, Jagiello and Atwell[19] estimated the spontaneous mutation rate of *Tfm* to be $0.4\text{–}0.5 \times 10^{-5}$ per generation; also compatible with the view that the mammalian genome contains only one gene locus which can mutate to give this particular phenotype.

The nature of control exercised by this single locus in target cells can be ascertained by comparing affected *Tfm*/*Y*☿ with +/*Y*♂ and +/+ ♀.

Tfm Mutation

Target organs of testosterone usually studied are seminal vesicles and prostates, but these organs are not present in +/+ ♀ and are missing in *Tfm*/*Y*☿. Accordingly, differences in the response to testosterone between +/*Y*♂ and +/+ ♀, on the one hand, and *Tfm*/*Y*☿, on the other, are studied on preputial glands in the case of rats[20] and on proximal tubule cells of the kidney in the case of mice[21–24]. Proximal tubule cells of the postnatal kidney are closely related ontogenically to Wolffian duct cells as both originate from the nephric blastema.

A single injection of as little as 1 mg of testosterone or 5α-dihydrotestosterone into +/+ ♀ or castrated +/*Y*♂ causes a 100 times induction of kidney alcohol dehydrogenase (E.C. 1.1.1.1) and β-glucuronidase (E.C. 3.2.1.31). Testosterone seems to remove the translational block from pre-existing mRNAs, as 5α-androstan-3α-17β-diol which is found only in the cytoplasm can effectively substitute for testosterone as an inducer[22,23]. Steroid hormone induction of specific enzymes in general seems to involve the removal of a translational rather than transcriptional block[25]. In *Tfm*/*Y* kidney, no induction whatsoever of these two enzymes occurs even after the administration of 20 mg of testosterone or 5α-dihydrotestosterone[21-23].

Most target organs hypertrophy in response to steroid hormones. Mouse kidney proximal tubule cells are no exception. The administration of 1 mg of testosterone or 5α-dihydrotestosterone causes 40 to 50% increase in the total kidney weight. Hypertrophy is apparently caused by the increased production of ribosomes on which translation of all the mRNAs depends. Testosterone concentrates in nucleoli of target cell nuclei[26] and stimulates a class of RNA polymerase which functions at a low ionic strength[27]. This is the RNA polymerase which is later identified as a specific RNA polymerase for transcription of rRNA genes in the nucleolar organizing region of the chromosome (nuclear RNA polymerase I of Roeder and Rutter[28]), it is likely that testosterone causes hypertrophy of target cells by either directly or indirectly stimulating RNA polymerase I. The stimulation by oestrogen of RNA polymerase I has been shown in rat uterus[29].

Tfm/*Y* ⚥ kidney remains atrophic even after the administration of 20 mg of testosterone or 5α-dihydrotestosterone[22,23].

Sixty minutes after an intravenous injection of 45 μCi of ^{3}H-testosterone, the *Tfm*/*Y* cytosol fraction contained 2,000 c.p.m./mg protein of testosterone, 100 c.p.m. of 5α-dihydrotestosterone and 400 c.p.m. of androstandiols. As the activities of the cytosol fraction of +/+ ♀ and +/*Y*♂ were no different, it was concluded that the *Tfm* mutation affected neither the uptake by the kidney cytoplasma of testosterone nor intracellular conversion of testosterone.

Amounts of testosterone-binding proteins in the kidney cytoplasma were assayed using ^{3}H-5α-dihydrotestosterone (DHT) in various concentrations. At a DHT concentration of 1.3×10^{-8} M, proteins in the cytosol fraction of +/+ ♀ and +/*Y*♂ bound 30×10^{-15} mol/mg protein of DHT after 60 min of incubation at 0° C, while the value for *Tfm*/*Y*⚥ was only one-tenth of that for +/+ ♀ and +/*Y*♂. It seemed that one class of testosterone-binding protein was entirely missing from the *Tfm*/*Y* cytoplasm[24]. As testosterone uptake by *Tfm*/*Y* cytoplasm was normal, the missing protein was clearly not a specific permease for testosterone.

The *in vivo* uptake of testosterone by kidney cell nuclei of *Tfm*/*Y*⚥ was grossly abnormal. No appreciable activity was detected 60 min after the intravenous injection of 45 μCi of ^{3}H-testosterone, while kidney cell nuclei of +/+ ♀ and +/*Y*♂ contained 500 c.p.m./10^{7} nuclei of testosterone. The relative deficiency of nuclear testosterone-binding protein was also noted. At a ^{3}H-DHT concentration of 3×10^{-8} M, proteins in *Tfm*/*Y* kidney cell nuclei bound 24×10^{-15} mol/mg DNA of DHT after an incubation of 2 h at 30° C, while a three times greater binding was observed in the kidney cell nuclei of +/+ ♀ and +/*Y*♂[24].

RNA Polymerase I

On the basis of these findings, I propose that inside the target cells of testosterone a protein specified by the wild type allele of the *X*-linked *Tfm* locus has a dual role. When it is not bound to testosterone, it stays in the cytoplasm and serves as a repressor of the translation of certain enzymes. Binding with testosterone or its metabolites changes its allosteric configuration, so that the bound form detaches from these mRNAs, releasing a translational block, and moves into the nucleus where it activates RNA polymerase I inside the nucleolar region (Fig. 2). In this way, a single gene product mediates the entire testosterone-induced response of target cells. Therefore, the loss of this binding affinity to testosterone by mutation simultaneously abolishes responses from all the target organs of testosterone. While testosterone causes hypertrophy in most target organs (activation of RNA polymerase I), different sets of enzymes are induced by testosterone in different target organs of the same species as well as in homologous target organs of different species. In the mouse kidney proximal tubule cell cytoplasm, the *Tfm* protein must be recognizing a short stretch of base sequence homologous in mRNAs of alcohol dehydrogenase and β-glucuronidase. In other target cell cytoplasm, mRNAs for these two enzymes may be absent. Instead, the *Tfm* protein may recognize a similar base sequence on mRNAs of other enzymes.

Proteins in the target cell cytoplasm which have a binding affinity to a steroid hormone have customarily been called cytosol receptor proteins, and it seems that the cytosol receptor protein moves into the nucleus and becomes a nuclear receptor protein[30,31]. In the case of target cells of testosterone, I propose that the so called cytosol as well as nuclear receptor proteins include a protein specified by the wild type allele of the *X*-linked *Tfm* locus as the most important component.

According to my scheme, the mammalian genetic regulatory system which governs the expression of sexual phenotypes is as simple as or even simpler than the *lac* operon system of *E. coli*. I believe that most other inducible regulatory systems of mammals are equally simple.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Radio Spectrum of Cygnus X-1

RECENT observations at 2,795 MHz with the NRAO interferometer[1] and at 1,415 MHz with the Westerbork array[2] have shown that a point radio source appeared in the field of the X-ray source Cyg X-1 some time between March 22 and April 28, 1971. On the basis of strong variability and close proximity, this radio source is identified with Cyg X-1 (refs. 1, 2). Observations with the NRAO interferometer at 2,695 MHz have shown that the source appeared constant in flux from May 13 to July 10, 1971.

We wish to report further observations of Cyg X-1 at 2,695 and 8,085 MHz with the NRAO interferometer and observations at 10,630 MHz with the 150 foot antenna at Algonquin Park, using a beam-switching technique. The results of these observations, together with the results of Braes and Miley, are shown in Fig. 1.

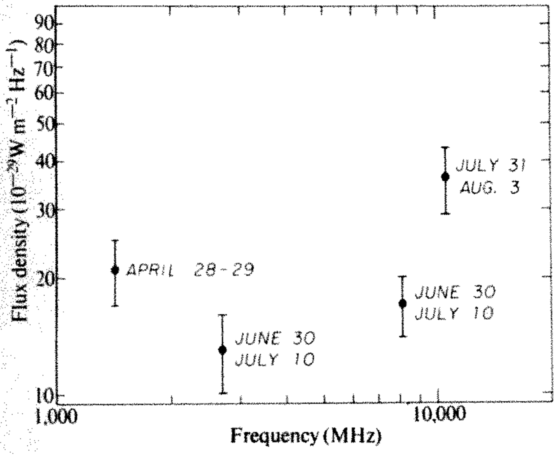

Fig. 1 The radio flux density of Cyg X-1 as a function of frequency. Dates of observation are shown for each data point.

Even though constancy in the radio flux at 2,695 MHz is well established, constancy is not yet established at 8,085 and 10,630 MHz. If, however, no variation has occurred at any frequency between April 28 and August 10, Fig. 1 shows that Cyg X-1 has a peculiar spectrum. Spectra like this are common in quasi-stellar sources (4C39.25, 3C279)[3] and some peculiar radio galaxies (3C84)[3], although the rise at the higher frequencies is rather steeper. Further spectral observations at many frequencies, but at the same time, are clearly needed so that the possible effects of time variation on the spectrum in Fig. 1 can be confirmed or eliminated. The simultaneous observations at 2,695 and 8,085 MHz do show signs of the high frequency turn-up clearly indicated a few weeks later at 10,630 MHz.

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Mineralogy of Apollo 15415 "Genesis Rock": Source of Anorthosite on Moon

PETROGRAPHIC, microprobe and X-ray data were obtained from thin section 15415,14 and 1–2 mm fines 15415,28, part of the anorthositic rock returned by Apollo 15. The section consists of ~97% coarse (1–4 mm) plagioclase and ~3% pyroxene associated with a trace of ilmenite. The pyroxene occurs as small (~0.05 mm) blebs both within and between plagioclase grains; in addition, several larger (~0.6 mm) pyroxene grains occur along boundaries. The fines consist of ~98% plagioclase with the rest being glass spheres and soil particles. Electron microprobe analyses were made of ten plagioclase points and ten pyroxene grains using standard procedures[1].

Table 1 Pyroxenes; wt. % Oxides; Mol % End Members

	Group 1		Group 2*	
	No. 1	No. 2	Average	Range
Na_2O	0.0	0.0	0.03	0.01–0.04
MgO	19.6	19.8	14.0	13.7–14.3
Al_2O_3	0.63	1.43	1.32	0.97–1.51
SiO_2	51.0	51.7	52.2	51.7–52.6
CaO	1.16	1.70	21.6	20.8–22.8
TiO_2	0.24	0.20	0.54	0.39–0.70
CrO	0.15	0.14	0.22	0.19–0.26
MnO	0.50	0.51	0.26	0.23–0.31
FeO	27.2	26.6	9.1	8.0–10.0
Sum	100.5	102.1	99.3	98.2–100.1
En	55	55	40	39–41
Wo	2	3	45	44–47
Fs	43	42	15	13–16

* Data for eight analyses averaged.

The plagioclase analyses show an unusually high average An content of 97.6 (range—$An_{96.7}$ to $An_{99.0}$), while minor elements have uniformly low concentrations, K 0.02, Fe 0.095, and Mg 0.035 per cent by weight. A single crystal from the fines showed sharp (b) and (c) X-ray diffractions characteristic of primitive anorthite. Polarized optical study of the thin section showed frequent, irregular twinning of the plagioclase, whose boundaries moved under pressure from a needle. Such elastic mechanical twinning is characteristic of anorthite[2]. Probably the irregular optical extinction and at least some of the twinning developed from mechanical deformation at the Moon's surface.

The pyroxene analyses consist of two distinct groups (eight augites and two low-Ca pyroxenes of undetermined symmetry) each with little compositional variation (Table 1). X-ray scanning images for FeK_{α} and CaK_{α} showed no detectable intergrowths in the larger pyroxenes, but one of the smaller blebs consisted of an intergrowth 10 μm in scale as shown by the Fe scanning image of Fig. 1.

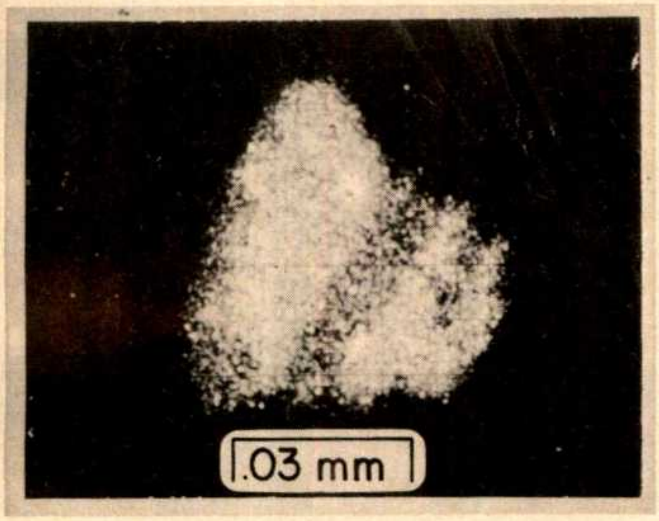

Fig. 1 FeK_{α} X-ray scanning image of pyroxene intergrowth. Light colour, low-calcium pyroxene; medium-light, high-calcium pyroxene; black, host plagioclase.

Fig. 2 is a plot of the normative constituents $CaSiO_3$ (Wo), $MgSiO_3$ (En) and $FeSiO_3$ (Fs) for the pyroxenes with respect to composition ranges found for Apollo 11, 12 and 14 specimens. The composition gap is greater than for any other pair of coexisting pyroxenes in a holocrystalline rock yet found on the Moon. Because the pyroxenes consist largely of separate grains, this suggests crystallization (or recrystallization) at a relatively low temperature with respect to the mare basalts. Rather than surface volcanism, one must look to deep-seated plutonic or to metamorphic processes.

The plagioclase is more calcic than any other yet found for holocrystalline rocks on the Moon, and both its major and minor elements agree well with a prediction made on the basis of studies of plagioclase from Apollo 11 and 12 rocks[3]. Fig. 3 summarizes the variation found between weight % Fe and mol % Ab ($NaAlSi_3O_8$) in plagioclases from mare basalt and exotic material from the fines (the latter probably corresponding to much of Apollo 14 material). Smith noted[3] that the data areas appeared to diverge from a composition near $An_{97}Ab_3$: K 0.03, Fe 0.1, Mg 0.01 weight %, a value consistent with that for rock 15415. He stated that "... it is tempting to speculate that the above composition may represent a source material common to all populations of both Apollo 11 and Apollo 12 material, while more sodic varieties represent the products of crystal-liquid differentiation under plutonic and volcanic conditions further modified in some instances by metamorphism".

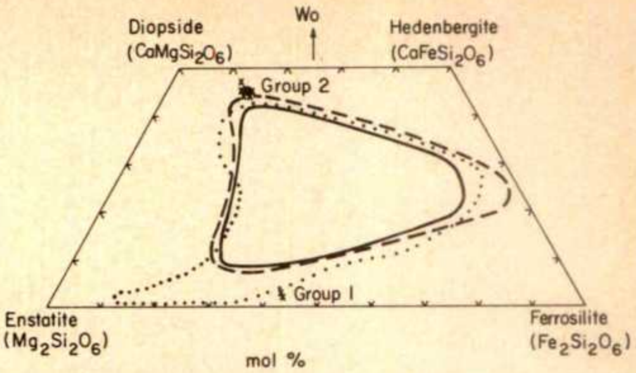

Fig. 2 Generalized plot of pyroxene compositions for Apollo 11 (- - -), 12 (——) and 14 (· · ·) from many sources. Pyroxene analyses from 15415,14 are indicated by crosses.

If rock 15415 represents an early differentiate of crystal-liquid fractionation producing feldspar-rich rocks from pyroxene-rich magma, one would expect the pyroxenes to be Mg-rich. The pyroxenes from 15415 are indeed more Mg-rich than the majority of pyroxenes from mare basalts, but they are less Mg-rich than some others, notably those from fines and exotic fragments. Perhaps some of these result from an earlier stage of differentiation, before plagioclase began to crystallize, while others result from late-stage accretion.

The discovery of plagioclase-rich fragments in Apollo 11 fines led to suggestions of extensive crystal-liquid differentiation producing an anorthositic crust[4] or a lunar crust composed of a mixture of plagioclase-rich rock, basalts and minor ultramafic material[5]. No evidence of cumulate textures has yet appeared to support these suggestions which require that plagioclase crystals float in a basaltic liquid. The plagioclase in 15415 does not show cumulate texture either. Perhaps metamorphism has obliterated earlier textures, but we wish to quote other evidence that argues against Earth-type crystal-liquid differentiation as the source of the plagioclase-rich fragments in Apollo 11 fines. For terrestrial igneous intrusions of basaltic composition, the $NaAlSi_3O_8$ content of the plagioclase increases with the Fe_2SiO_4(Fa) content of the coexisting olivine as shown for four intrusions listed in ref. 6 (Fig. 4). Five fragments from Apollo 11 listed in ref. 7 show a trend sloping in a quite different direction, with Fa of the olivine decreasing as Ab increases in the plagioclase. The olivine and and plagioclase solid solutions are supposed to be nearly ideal at liquidus temperatures, so there is no simple explanation of this trend on the basis of crystal-liquid fractionation analogous to that seen in terrestrial intrusions. One possibility is extensive

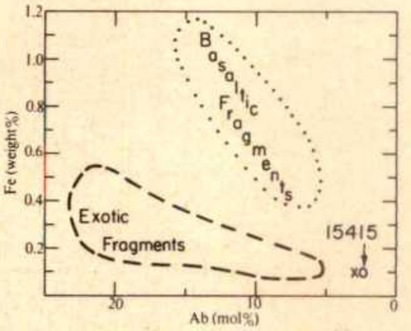

Fig. 3 Generalized plot of Fe (weight %) versus Ab (mol %) for Apollo 12 rocks. Dashed area, breccia and grey-mottled fragments; dotted area, basaltic fragments 12070,145 and 12010,31. Apparent intersection marked by cross, observed composition in 15415,14 by circle.

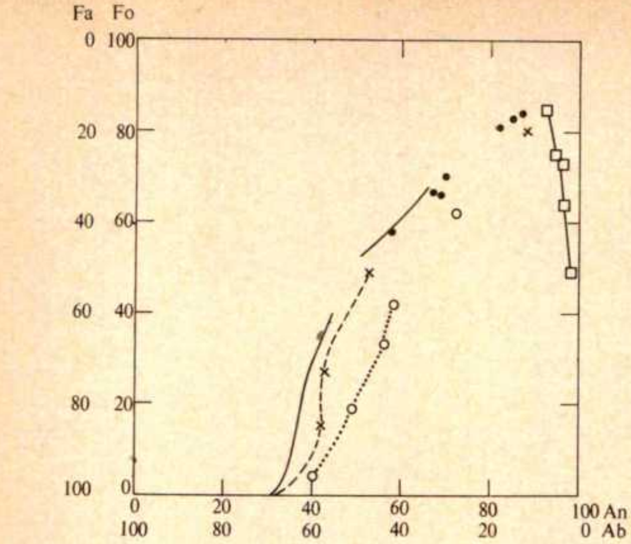

Fig. 4 Ab content (mol %) of plagioclase against Fa content (mol %) of coexisting olivine in terrestrial igneous intrusions of basaltic composition and in plagioclase rich fragment from Apollo 11 fragments. ——, Skaergaard; ×, Buchveld; ○, Insch; ●, Cullin; □, Apollo 11.

volatilization from lava lakes[8] which should deplete the sodium in preference to the calcium, perhaps while the content of ferrous iron was increasing in the liquid.

At this time, it is obvious that the feldspar-rich rocks from the Apollo 11 mission pose difficult problems, and it remains to be seen whether rock 15415 is correctly named the "genesis rock".

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Regular Pulses from the Sun and a Possible Clue to the Origin of Solar Cosmic Rays

A CURIOUS but rare feature of the metre-wave continuum (type IV) radiation received from certain large solar flares is the pulsating structure which modulates the intensity in a periodic or quasi-periodic manner[1,2]. The modulation may persist for about 1 min or more and the period of the pulsation is typically of the order of 1 s. Of various explanations suggested, we consider the most satisfactory to be that of Rosenberg, in which the radiation is attributed to synchrotron radiation emitted by electrons in a magnetic flux tube embedded in the solar corona and the pulsations are attributed to modulation by standing magnetohydrodynamic (MHD) waves set up within the tube. We now present further evidence of this phenomenon and outline a model which accounts both for the acceleration of the emitting electrons and for the pulsations themselves. There is also evidence to suggest that energetic protons may be accelerated by the same process. We consider that the phenomenon affords a possible observational clue to a physical process by which solar cosmic rays can be generated high in the solar corona.

Our work was stimulated by an extraordinary pulsating event recorded with the Culgoora radiospectrograph on September 27, 1969 (Fig. 1). A remarkably regular series of about 50 sharp pulses were received in the frequency range 100 to 200 MHz, each pulse occurring almost simultaneously throughout the frequency range. The interval between pulses varies slowly from 2.5 to 2.7 s during the lifetime (2.5 min) of the pulse train. The pulses appear as a deep modulation of the middle part of an otherwise smooth rise and fall of continuum (Fig. 2).

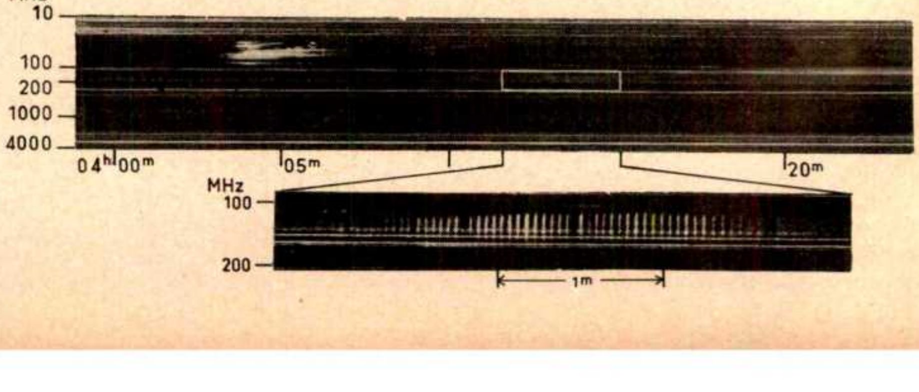
The pulses begin 25 min after the start of a large flare. The production of a type II burst (Fig. 1) signifies[3] the generation of a shock wave and its passage through the corona. Because the fundamental band of the type II burst had, at the time of the pulsations, drifted down to a frequency of about 30 MHz, the shock wave was then at a height of about 1.5 $R_\odot$.

A search through our records revealed seven other instances of pulsations. All but one were accompanied by type II bursts and occurred at a time when the shock wave had reached a height of between 1 and 2 $R_\odot$.

In an effort to interpret this phenomenon, we have sought a physical model which accounts for (1) the extreme regularity and sharpness of the pulses; (2) the fact that the pulses modulate part of a longer rise and fall of continuum; and (3) the occurrence of the first pulses at the time that a shock wave passes through a height level of $\gtrsim 1\ R_\odot$. The most plausible model is illustrated in Fig. 3. We presuppose the existence of a well defined magnetic flux tube with its feet in the photosphere and its top high in the corona; several pieces of radio and optical evidence point to the formation of such magnetic arch structures or loops above flare regions.

The shock wave from the flare expands and at some stage interacts with the flux tube (Fig. 3*a*). The shock front compresses the magnetic field in the two regions where it crosses

Fig. 1 Dynamic spectrum record of the pulsed event of September 27, 1969. A type II burst is clearly visible at the start of the event, and the second harmonic continues faintly at frequencies less than 60 MHz during and after the pulsed part of the event. The pulses occur in the part of the record enclosed by a white box and a high contrast enlargement of this section of record is reproduced in the bottom half of the figure to show the pulses more clearly.



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[2] Fraenkel-Conrat, H., in *Comprehensive Biochemistry* (edit. by Florkin, M., and Stotz, E. H.), **7**, 75 (Elsevier, Amsterdam, 1963).

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the flux tube and generates large amplitude Alfvén wavetrains which travel up and around the loop in each direction. We assume that the magnetic field inside the loop is so much greater than the field outside the loop that the Alfvén waves travel several times faster than the shock itself. Thus the length of the tube above the shock soon becomes filled with the intermingled pair of oppositely directed wavetrains. This physical situation is one suited to the acceleration of electrons by the Fermi process as discussed by Parker[4] and Wentzel[5]. The electrons gain energy at repeated reflexions between converging waves, the pitch-angle distribution of the electrons being maintained by scattering on the sharp crests which develop on waves with large amplitudes. The increasingly energetic electrons at the top of the arch become the source of synchrotron radiation of increasing intensity and so account for the initial rise in the level of continuum radiation.

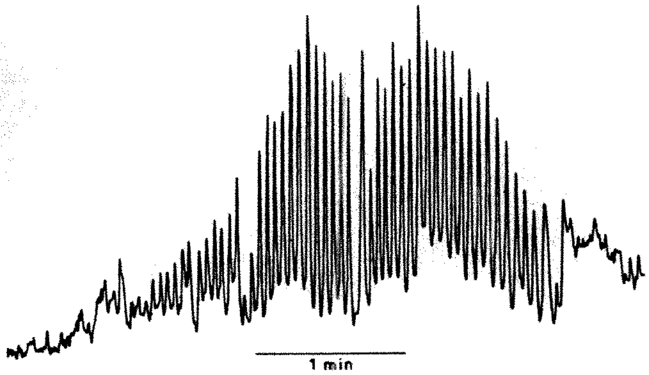

Fig. 2 Microphotometer trace along the spectral record of Fig. 1 showing the variation with time of the intensity of radiation received at 150 MHz.

A new situation can develop when the shock front reaches the top of the arch (Fig. 3*b*), for then the front can be aligned nearly parallel to the flux tube over a length which is large compared with the tube diameter. Under this condition the tube is excited into radial oscillations of the kind discussed by Rosenberg[2], the magnetic field oscillations giving rise to oscillations of the intensity of the synchrotron source. We have made calculations which demonstrate that small variations in the magnetic field can produce considerably larger variations in the intensity of synchrotron radiation. The steep dependence of intensity on magnetic field thus allows the generation of sharp, deeply modulated pulses even if the magnetic oscillations are sinusoidal and relatively weak.

After the shock front has cleared the loop (Fig. 3*c*) the energetic electrons are gradually lost from the source as they diffuse back down the field lines towards regions of higher density where the medium suppresses the synchrotron emission. During this phase there is a gradual decay of the continuum.

The transition from pulsations to final continuum is very abrupt, and the continuum seems to be continuous with the envelope of pulse maxima. With the possible exception of these two puzzling details, we believe that we have explained all the basic features of this burst.

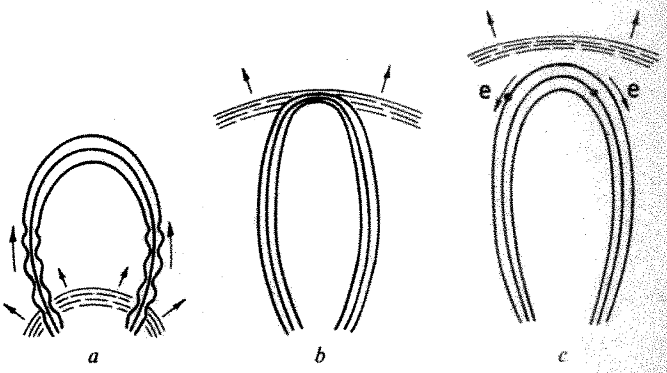

Fig. 3 Diagrams illustrating the geometry of the mechanism proposed to explain the event of Figs. 1 and 2. The three diagrams represent successive stages of the upward expansion of a shock wave and its interaction with a discrete magnetic flux tube.

This model can be explored quantitatively with the aid of several important observable parameters relevant to the maximum phase of the pulsations, namely the period of the pulsation τ, ≈ 2.5 s; the plasma frequency (from type II burst) $f_p \approx 30$ MHz; the peak frequency of synchrotron emission f_m, ≈ 150 MHz; and the maximum flux density S, $\approx 5 \times 10^{-21}$ W m^{-2} Hz^{-1}, measured at the frequency f_m.

If d is the diameter of the flux tube, l the effective length of the tube contributing to the pulsations, T_B the peak brightness temperature of the source, E the kinetic energy of the radiating electrons (assumed mono-energetic), $f_B = eB/2\pi m_0 c$ the mean electron gyro frequency and $v_A \approx 7 \times 10^3 \, f_B/f_p$ the Alfvén wave velocity, we may make use of the relations

$$\tau \approx d/v_A$$

$$kT_B \approx 0.5c^2 \, D^2 \, S/(ld \, f_m{}^2)$$

$$E \gtrsim kT_B$$

where D is the distance between the Sun and the Earth and k is Boltzmann's constant. We also make use of an approximate form[6] of the formulae for synchrotron radiation to relate f_m to E and f_B and f_p. Assuming $l \approx 10d$ we have derived, with the aid of some numerical computation, the following

Table 1 Comparisons with Solar Proton Observations

Date	Flare Time of maximum (UT)	Coordinates	Imp.	Cosmic-ray increase Date	UT	Delay (h)
June 27, 1960	0010	S10 E33	3	No data		
February 24, 1969	2316	N12 W32	2B	February 25	1000 to 1100	(~11)*
September 27, 1969	0412	N09 E02	3B	September 27	0900	5
April 8, 1970	2333	N15 E55	SN	No increase		
June 30, 1970	0316	N18 E56	SN	No increase		
November 5, 1970	0320	S12 E37	3B	November 5	0200 to 0800	<5
December 11, 1970	2215	N16 W00	2N	December 12	0900	7
January 25, 1971	2309	N19 W49	2B	January 25	2366	0.5

* A second flare starting at 0903 on February 25 was a more likely cause of this proton event. Apparently the second flare was associated with the pulsed radio event described by Rosenberg[2].

quantities: $d \gtrsim 0.02\ R_\odot$; $E \lesssim 0.8$ MeV; $B \gtrsim 6$ gauss; $v_A \gtrsim 4 \times 10^3$ km s^{-1}; $T_B \lesssim 10^{10}$ K. All these values seem to be within reasonable bounds if it is appreciated that the somewhat high value of magnetic field refers to the highly localized resonating flux tube, which is likely to contain strong electric currents and twisted fields.

Further important considerations were suggested by the model—for example, the Fermi process invoked to accelerate the electrons may also be effective in accelerating protons in the same region. To test this idea we examined the reports of satellite observations of solar protons[7] for all eight pulsating events recognized from our data (see Table 1). Four of the seven events for which proton data were available were associated with proton emission and, in a fifth case, there is a possible association. The other two were at large eastern longitudes and were thus unfavourably located for the detection of protons. We consider that this result represents *prima facie* evidence for an association between the radio pulsations and the acceleration of protons. The same basic particle accelerator that we are proposing—that is the interaction of a shock or other MHD wave with a discrete arch-shaped magnetic flux tube—may explain why synchrotron sources are seen—on radioheliograph records—to become concentrated at the top of magnetic arches[8]. A similar mechanism may also be responsible for the acceleration of particles at lower heights in the solar atmosphere and, indeed, for other astrophysical phenomena.

We thank Dr S. F. Smerd for criticism of this work.

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What Flux Limits can be Set for X-ray Pulses accompanying Weber's Pulses?

THE vast ratio, $\sim 10^{-40}$, between gravitational and electromagnetic forces has prompted two groups[1,2] to search for radio pulses which might accompany the pulses reported by Weber[3,4]. In view of the restricted bandwidths in the radio experiments, and uncertainties about the dispersion in the interstellar plasma, I discuss here the sensitivities that might be attained in other regions of the electromagnetic spectrum.

X-ray satellites[5] could in principle be used to look for occasional bursts of X-rays, but with an expected event rate of ~ 1 day^{-1} (ref. 4), it is unlikely, however, that they could be spared for the necessary long periods of observation. Moreover, many of the satellite instruments have narrow beams, and use spin and precession to achieve all-sky coverage.

This letter draws attention to the potential of the upper-air X-ray fluorescence technique[6-9], which is ground-based, cheap, has a wide input energy bandwidth, and is non-directional. The latter feature is particularly important, as the "beamwidth" of Weber's existing detector is $\sim 70°$ (ref. 4). How small a fraction of the energy in the pulses of gravitational radiation (GR) would have to be emitted in the X-ray band to be detectable by this method, assuming that GR events arise from collapsing objects at the galactic centre? The question of the time-scale is vital. A collapsing object of mass $\sim 10\ M_\odot$ would emit a GR pulse of duration ~ 0.1–1 ms[10], but the emission of any electromagnetic radiation would in general be much longer, arising, as it must, from the outer regions of the object. On the shock-wave model of supernovae[7], however, prompt X-rays are expected on exceedingly short time-scales, $\sim \mu$s. Several models of stellar collapse[11-13] suggest that the bulk of the prompt emission of energy from a typical collapsing star emerges on a time-scale in the region 0.1–3.0 s.

Consider a single large phototube of area A and quantum efficiency, ε_p viewing the entire (2π) solid angle of sky, set up to detect an X-ray burst of flux-level φ_x through the 3914 Å fluorescence band of the N_2^+ ions in the upper atmosphere. If the fluorescence conversion efficiency is ε_f, and the integration time constant τ is arranged to match the duration of the burst, the signal to noise ratio (S/σ) is given by[14]

$$(S/\sigma) = (\varphi_x\ \varepsilon_f / 2h\nu_{3914}) \,.\, (A\varepsilon_p/\varphi_B \tau)^{\frac{1}{2}} \qquad (1)$$

where φ_β is the background light from the night sky, integrated over the hemisphere.

Inserting $\varphi_B = 1.55 \times 10^9$ photons s^{-1} (3500–5000 Å) (ref. 15), $A = 730$ cm^2, $\varepsilon_p = 0.15$ (S-11 cathode), $h\nu_{3914} = 3.1$ eV, and $\varepsilon_f = 10^{-3}$ (ref. 16) (the average value over $E_x \sim 10$ keV–100 keV) in (1), integrating over $\tau = 0.1$ s, and demanding a signal $S = 15\ \sigma$ (that is, roughly three times peak-to-peak noise), the limiting detectable X-ray flux is

$$\varphi_x = 1.8 \times 10^{-4} \text{ erg cm}^{-2} \text{ (event)}^{-1}, \text{ in the band 10–100 keV} \qquad (2)$$

If we take Weber's result to indicate a GR-flux $\sim 10^4$ erg cm^{-2} (event)$^{-1}$ in his bandwidth, then an associated X-ray burst would escape detection in this exceedingly simple detector, only if

$$\varphi_x \leq 1.8 \times 10^{-8}\ \varphi_{GR} \qquad (3)$$

The intrinsic input bandwidth of a fluorescent receiver is 100 eV–100 keV (ref. 9), but photoelectric absorption in the interstellar medium will eliminate the lower energy regions. Taking a column density $\int n_H\, dl = 1.5 \times 10^{22}$ atoms of atomic hydrogen cm^{-3} toward the galactic centre[17] ($d = 8.2$ kpc), and the absorption spectrum of Bell and Kingston[18], the opacity of the interstellar medium to the galactic centre is unity for $E = 1.7$ keV. Taking a conservatively lower energy limit of $E = 5$ keV, we thus ensure that the absorption is insensitive to the abundances of H_2, He or Ne, about which there is still some discussion[19]; Compton scattering is also negligible[19]. There may also be a local dense cloud around the site of Weber's reported events which would yield a higher than average column density.

Scattering by dust causes both attenuation and time dispersion of X-ray pulses from distant sources[20], and is more difficult to assess, but some tentative estimates of time-dispersion can be made from existing observations of X-ray sources near the galactic centre. Absorption and scattering cannot be too severe, for at least eleven point sources have already been discovered in the direction of the galactic centre[21], and their angular diameters are $< 1.5'$. Assuming that this figure represents an upper limit to the diameter of a halo caused by dust scattering, and using the nomenclature in ref. 20, then $\theta \sim 3'$, at the geometric mean energy 3.3 keV of the energy band used by the MIT group[21].

Extrapolating to the geometric mean energy of the proposed fluorescent detector, that is 22 keV (for 5–100 keV) I deduce, since $\theta \propto \lambda$, the corresponding scattering angle $\theta \sim 1.6 \times 10^{-5}$ radians, so that the time dispersion δt, again from ref. 20, is $\delta t \sim D\theta^2/32c$. With $D = 8.2$ kpc, $\delta t \sim 6.6$ s. Increasing τ from 0.1 s to 7 s, in (1), the sensitivity is lowered by $\sqrt{70}$, that is, by roughly one order of magnitude; sky transparency fluctuations may well then set the limit of performance on such a time-scale. The above arguments necessarily depend on the composition, dimensions, and number-densities of the particles involved.

In spite of this estimate, however, if the optical extinction coefficients are any guide, the effects of dust scattering may be more severe. It has been estimated[22] that in the visible region $A_v = 2$ mag for the pulsar NP 0532 at $D = 2$ kpc, while for the galactic centre ($D = 8.2$ kpc), A_v may be as large as 25 mag (ref. 23), or even 29 mag (ref. 24), if the extrapolations from the infrared are reliable. The relevance of these figures to the present discussion on X-ray scattering nevertheless depends critically on the sizes of the particles or grains.

There is already evidence[14,25] that light pulses of unknown origin are detected from the night sky, on time-scales ~50 μs–1 ms, though such light receivers have not yet been operated with the much larger integrating times (~0.1 s) suggested here.

When lists of the times of occurrence of GT events are published by Weber or others, a single night-sky fluorescent receiver may be sufficient to set a low limit on the X-ray flux accompanying these events. In the absence of such published data, however, more complicated installations would be necessary, involving widely spaced light receivers operating in coincidence. To observe the galactic centre with reasonable efficiency, these ground-based X-ray experiments should be carried out in the southern hemisphere or at low latitudes in the northern hemisphere, at desert or mountain sites, which are free from interference from a.c. lighting and man-made sources of pulsed light.

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BIOLOGICAL SCIENCES

Electron Density Profiles of Nerve Myelin

THE structure of the nerve membranes within the myelin sheath of frog sciatic nerve has been studied by low-angle X-ray diffraction. Many additional orders of diffraction have been recorded from nerve, and, from a structure analysis of this new X-ray data, a twelve-parameter electron density model is proposed. Fourier series representations of the one-dimensional electron density of live nerve myelin at two different resolutions are also presented; these resolutions are 7 Å and 4.8 Å.

It has been known for some time that the low angle X-ray diffraction pattern of peripheral nerve myelin[1,2] shows the first five diffraction orders ($h = 5$) of a radial repeat distance $d = 170$–185 Å depending on the variety of nerve. The radial repeating unit is derived from two plasma cell membranes which form the membrane pair. The interpretation of the low angle X-ray diffraction intensities from nerve leads to a description of the one-dimensional electron density distribution in a radial direction at right angles to the surface of the myelin sheath. The effective resolution Δx of a Fourier series representation of this electron density is given by $\Delta x = d\,(2h)^{-1}$ where d is the radial repeat distance and h the number of diffraction orders used in the synthesis. The low angle X-ray diffraction pattern of frog sciatic nerve[1,2] had $d = 171$ Å, $h = 5$, and hence the effective resolution is only moderate, namely, $\Delta x = 17$ Å. Many additional orders of diffraction, $h = 18$, have been recorded, however[3,4], and the effective resolution of a Fourier synthesis is now considerably better as $\Delta x = 4.8$ Å.

This resolution will only be meaningful if the correct phase can be found for each order of diffraction. Fortunately, the radial repeating unit seems, from the way the myelin sheath is generated from the Schwann cell membranes, to have a centre of symmetry. This means that the phase of each diffraction order can only be + or −. Thus, there are 2^h different ways of assigning phases to the h orders of diffraction. Different methods of structure analysis have been used at various times in an attempt to solve the phase problem and so obtain a valid description of nerve myelin structure. These methods are as follows: (1) swelling experiments to trace the Fourier transform[5–9]; (2) model building to choose between certain kinds of possible electron density models[7,9–11]; (3) examination of Patterson difference function[11]; (4) examination of Fourier difference densities; (5) the use of the sampling theorem to examine two or more closely related sets of X-ray data from nerve, and the use of the sampling theorem as a method of analytic continuation[12]; (6) examination of the X-ray patterns from swollen and shrunken frog sciatic nerve[8].

We have developed a twelve-parameter electron density model[15] for nerve, in which we use the following notation: d, radial repeat distance; v, thickness of the membrane pair; c, thickness of the cytoplasmic fluid layer composed of electron density F; d-v, thickness of the extracellular fluid layer composed of electron density F; l, thickness of the layer composed of electron density L; i_1 and i_2, thicknesses of the layers composed of electron density I; p_1 and p_2, thicknesses of the layers composed of electron density P; s, thickness of the layer composed of electron density S. The electron densities have the

Table 1 Model Phases for the First Twelve Diffraction Orders

Kind of model $h =$	1	2	3	4	5	6	7	8	9	10	11	12
Five-parameter	−	+	+	−	−	+	+	−	−	+	+	+
Seven-parameter	−	+	+	−	−	+	+	−	+	−	−	−
Eight-parameter	−	+	+	−	−	+	+	−	+	−	−	−
Twelve-parameter	−	+	+	−	−	+	+	−	+	−	−	−

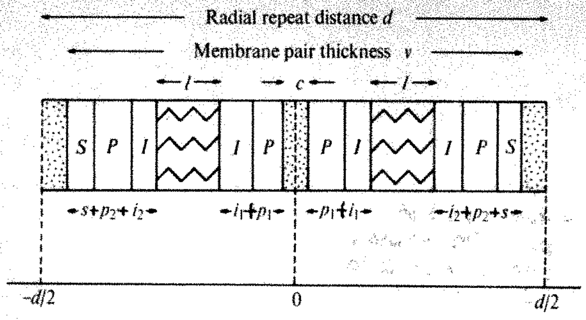

Fig. 1 The twelve-parameter electron density model is centrosymmetrical and contains two asymmetric nerve membrane units per radial repeat. The clear regions refer to electron densities *P*, *I* and *S*, the zigzag lines refer to electron density *L* and the dotted regions refer to the fluid electron density *F*. The thickness of a single nerve membrane unit is given by $p_1+i_1+l+i_2+p_2+s$.

following variation: *P* is high, *I* is moderately high, *S* is moderate whereas *L* is low. The twelve parameters are the five electron densities (*F*, *P*, *I*, *L*, *S*) and the seven layer thicknesses (c, p_1, p_2, i_1, i_2, l, s) but, because fluid density *F* is known and because X-ray intensities are on a relative scale, there are only ten operational parameters. In order to describe electron densities in terms of electrons per Å^3 additional considerations are required and have been described elsewhere[9,13]. The following model parameters for frog sciatic nerve were obtained: $P=0.37$ electrons per Å^3, $I=0.36$ electrons per Å^3, $L=0.27$ electrons per Å^3, $S=0.35$ electrons per Å^3, $c=10$ Å, $p_1=13$ Å, $i_1=10$ Å, $l=21$ Å, $i_2=9$ Å, $p_2=12$ Å, $s=10$ Å. A diagram of the twelve-parameter electron density model is shown in Fig. 1. The following properties of frog sciatic nerve myelin are noted. The thickness of a single membrane is 75 Å, which is similar to that of earlier models. The single membrane is asymmetric and this is similar to that shown by the seven and eight-parameter models. The thickness of the central low electron density region is unexpectedly narrow (as in the three earlier models) and the actual value of l is 21 Å; this region is thought to contain the lipid hydrocarbon chains. The thicknesses of electron density layers *I* and *P* have the property $i_1 \approx i_2$ and $p_1 \approx p_2$. The five layers therefore (p_1, i_1, l, i_2, p_2) form an approximate centrosymmetrical unit. The asymmetry of the nerve membrane unit arises primarily because of the presence of the moderate electron density layer which is 10 Å thick and faces the extracellular fluid space. This observation of a symmetrical unit within the nerve membrane suggests that these five layers may constitute a symmetric lipid bilayer with the protein component confined to only one layer, the 10 Å layer. Accordingly, a molecular model has been constructed and some of the details have been reported briefly[15].

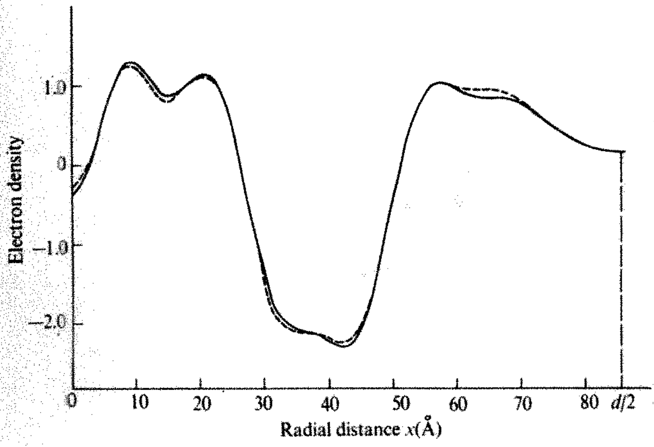

Fig. 2 Fourier series representations for the myelin layers of frog sciatic nerve computed using the first twelve reflexions. The continuous curve refers to the observed Fourier and the discontinuous curve refers to the calculated Fourier series. The Fourier syntheses are on the same relative scale.

The phases of the first twelve reflexions for four models[7,11,13,15] are shown in Table 1. The only difference is that the sign combinations of reflexions $h=9$ to 12 are reversed in the three later models. The strong $h=11$ reflexion has a negative phase in the three later models whereas it had the opposite phase in the 1968 model. A study using method (5) supports the choice of phases given by the later models. This study is independent of any model-building considerations. The Fourier series representation for nerve[14] is given by the series

$$\left(\frac{2}{d}\right)\sum_{l}^{h}\{\pm\}\,[J(h)]^{1/2}\cos 2\Pi hx/d$$

where $J(h)$ is the corrected X-ray intensity and $\{\pm\}$ refers to the phase information. Fourier syntheses calculated using $h=12$ and $h=18$ reflexions are shown in Figs. 2 and 3, respectively. The corresponding effective resolutions of these Fouriers are 7 Å and 4.8 Å, respectively. The continuous curves are the Fourier series representations for the myelin layers of frog sciatic nerve; they were computed using the observed X-ray diffraction intensities after corrections had been applied and the phases from the twelve-parameter model. The discontinuous curves are the Fourier syntheses calculated using the theoretical diffraction derived from the model together with the model phases.

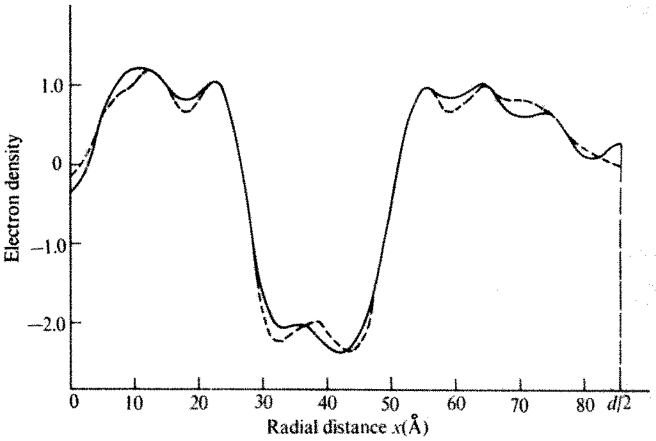

Fig. 3 Fourier series representations for the myelin layers of frog sciatic nerve computed using the first eighteen reflexions. The continuous curve refers to the observed Fourier series and the discontinuous curve refers to the calculated Fourier series. The Fourier syntheses are on the same relative scale.

To illustrate the agreement between the twelve-parameter model and the observed low angle X-ray data, it is convenient to show the corresponding Fourier series representations for live nerve. In Figs. 2 and 3 the observed and calculated Fourier syntheses ($h=12$ and $h=18$) show only small differences although the differences between the two electron density curves in Fig. 3 are more noticeable. The good agreement between the observed and calculated Fouriers suggests that the twelve-parameter model is a reasonable choice for nerve and therefore the parameters of this electron density model closely resemble the molecular parameters of live nerve.

It is appropriate to point out difficulties in trying to identify certain features of electron density curves with molecular parameters. For example, in Figs. 2 and 3, the Fourier series have a ripple contour superimposed on the true electron density of the nerve membrane; the wavelength of this ripple contour is approximately 2 Δx. The fact that the interpretation of such a Fourier series is not rigorous and presents obvious problems has been recognized[10]. We have tried to avoid those difficulties by starting with an electron density model. In this case the information contained within the observed Fourier synthesis can be examined by use of Fourier difference densities.

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Are Noradrenaline Excitations Artefacts?

IT has frequently been reported that noradrenaline applied by microiontophoresis depresses firing in neurones of the central nervous system[1–11]. Excitatory responses have also been found, however, both in cells which are, and in cells which are not, depressed by noradrenaline[12–19]. In the former case, depression is followed by a delayed excitation. In all cases excitatory responses are delayed and often reach a maximum after the end of the application, after which the cell does not recover its original firing rate for 2–3 min. Furthermore, the excitant effects of noradrenaline are stereospecific for *l*-noradrenaline and can be blocked by the common adrenergic blocking agents[12–14,18] whereas the depressant responses are not stereospecific and cannot usually be blocked by these agents[2,5, 8,12–14]. It has therefore been suggested that noradrenaline is an excitatory transmitter in the brain, and that the depressant effects represent a non-specific effect on cellular membranes or processes[14].

We have found that microiontophoretic application of noradrenaline causes small blood vessels to constrict with a latency and time course strictly comparable to the excitant effects of noradrenaline on some central nervous neurones. The experiments were carried out on arterioles less than 500μ in diameter of the intestine and mesentery of 300 g rats anaesthetized with urethane. Five-barrelled micro-pipettes were used for iontophoresis, and control experiments were carried out to check for *p*H or current effects. All drug solutions were 0.2 M in de-ionized water. Acetylcholine, acetyl-β-methyl choline, and sodium L-glutamate produced no apparent change of vessel diameter when ejected with currents of up to 300 nA.

Ejection of noradrenaline bitartrate produced a localized constriction of the vessels, the threshold for an observable effect on most vessels being at doses of about 20 nA. Maximal constrictions were obtainable with doses of approximately 100 nA. At intermediate doses an increase of ejecting current increased the resulting degree of constriction. The changes in diameter of an arteriole resulting from an 80 nA dose of noradrenaline are shown in Fig. 1. The typically long latency of the effect (noradrenaline retaining current only 10 nA) and the slow recovery are clearly apparent. The peak effect is attained after ending the noradrenaline ejection. Similar observations have been made recently in the frog[21].

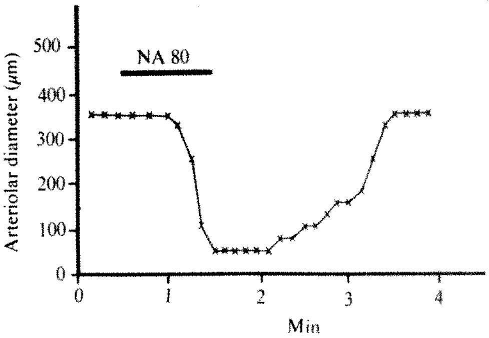

Fig. 1 A graph of the changes in the diameter of an arteriole against time as a result of an 80 nA dose of noradrenaline (NA80) applied by microiontophoresis. The long latency and slow recovery of the constriction are clearly seen.

We suggest that the neuronal excitatory effects of noradrenaline in some areas of the central nervous system may be secondary to effects on blood vessels. Indeed, it is not difficult to see a cause and effect relationship between vessel constriction and neuronal excitation. Constriction of a small blood vessel or capillary in the vicinity of a neurone soma would effectively reduce the availability of oxygen diffusing from the contained blood to at least a part of the cell. Furthermore, it has been known since the work of Lorente de Nó[22] that hypoxia will depolarize nerve fibres. Hence it seems reasonable to assume that the localized hypoxia resulting from constriction of a small blood vessel would at least increase the tendency to depolarization of a nearby neurone.

This effect might be rather weak, however, in the case of larger cells which may be receiving oxygen from several nearby vessels. This might explain the observation that noradrenaline excitations are often not apparent until a burst of firing is initiated in the cell under study by, for example, an excitant amino-acid. In such cases the amine excitation is often seen as a prolongation of the amino-acid effect.

This hypothesis can also be used to explain certain differences seen by workers using different anaesthetics. In the cat neocortex, for example, Krnjević and Phillis[7,20] using barbiturate-anaesthetized or unanaesthetized preparations observed depressant responses to noradrenaline normally, although higher doses occasionally elicited excitatory responses. Johnson *et al.*[14,15], however, noted excitatory effects of noradrenaline on 57% of the cells studied (compared with 20% depressed) during nitrous-oxide/halothane anaesthesia, and observed that administration of 0.5% halothane would potentiate excitatory responses of cells in barbiturate-anaesthetized animals, and would cause previously unresponsive cells in unanaesthetized animals to be excited by noradrenaline. Phillis and York[9] in the same tissue observed a much smaller proportion of excitant effects (49% depressed) when using nitrous-oxide/methoxyflurane anaesthesia. Increasing the depth of halothane anaesthesia below a moderate level also reduces the incidence of excitant responses[15].

Now, a study of blood vessel reactivity during anaesthesia[23] revealed that the response of small vessels to catecholamines is greatly enhanced during light halothane anaesthesia, is less during deep halothane anaesthesia, and is greatly reduced during methoxyflurane anaesthesia. Blood vessel responsiveness, therefore, correlates with the proportion of excitant responses seen with different anaesthetics.

The marked similarities between the pharmacology of noradrenaline excitation in the central nervous system, as mentioned earlier, and peripheral adrenergic pharmacology lend further support to the hypothesis. Some results are also available for agonist studies. For example, ergometrine, which has negligible vasoconstrictor activity peripherally, has no excitant effects on central neurones. Methylergometrine, however, which does have vasoconstrictor activity also causes some excitation of central neurones[20].

Thus, some excitatory effects of microiontophoretically applied noradrenaline in the central nervous system may be indirect effects secondary to localized vascular changes. This is not to say that all such effects are produced in this way, but great care in the interpretation of microiontophoretic studies is essential.

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Serum-mediated Immunological Non-reactivity between Histoincompatible Cells in Tetraparental Mice

THE capacity of a serum factor, probably antibody or antigen–antibody complex, to block expression of cell-mediated immunity to tumours has been clearly demonstrated[1,2]. This principle of blocked cellular immunity has been extended to account for the apparent tolerance between histoincompatible cells present in radiation[3] and neonatally induced bone marrow cell chimaeras[4]. It has been suggested that even self-tolerance might be due, not to the absence of self-reactive lymphocytes, but to the presence of a serum factor capable of blocking the reactivity of these lymphocytes[1]. Additional support for this notion has been obtained using tetraparental (allophenic) mice. The mice are derived from the fusion of two eight-cell embryos, a stage long before the immune system has appeared. The fused embryo is reimplanted into a pseudopregnant female and matures into an apparently normal adult. If the parents are of different strains, a chimaeric animal develops whose tissues contain cells of both parental strains. These animals are functionally tolerant to themselves and either parental strain[5]. A microcytotoxicity assay has been used[6] to demonstrate that there are lymph node cells in tetraparental mice which can kill parental strain cells *in vitro*, but the activity of which is presented by the presence of tetraparental serum. We have now extended the observation of blocking activity of tetraparental serum to mixed lymphocyte cultures (MLC) between parental strain cells. We also present preliminary results on the nature and specificity of the serum blocking factor.

Tetraparental mice were provided by Dr R. J. Mullen, Department of Neuropathology, Harvard Medical School. They were derived from the fusion of C57Bl/10 and SJL embryos using techniques previously described[7–9]. All mice showed coat colour chimaerism and were more than 1 yr old. Normal C57Bl/10, SJL, (C57Bl/10 × SJL) F_1 hybrid, BALB/c and CBA mice were obtained from Jackson Laboratories, Bar Harbor, Maine. Sera were stored at $-70°$ C and heat inactivated at 56° C for 40 min before use.

MLCs were carried out by the technique of Adler *et al.*[10] with modifications (S. M. Phillips, C. B. Carpenter and J. P. Merrill, manuscript in preparation). Culture tubes contained either 15×10^6 washed spleen cells of one strain, or 7.5×10^6 cells from each of the two responding strains in a final volume of 2 ml. The medium was RPMI-1640 containing 10% heat inactivated normal human serum, penicillin, streptomycin, and hepes buffer. In cultures where only one of the two strains could undergo DNA synthesis (one way MLCs), 15×10^6 spleen cells of the responding strain were incubated with 15×10^6 mitomycin-treated spleen cells from the non-responding strain[11]. Test sera were added to target cells 30 min before the addition of responding cells. The rate of DNA synthesis in each tube was assessed by adding 2 µCi of tritiated thymidine at 68 h of culture and determining its incorporation into DNA over the following 4 h. The proliferative response of spleen cells to phytohaemagglutinin (PHA) was measured at 48 h of culture. Tritiated thymidine incorporation was expressed either in c.p.m. or as an isotope incorporation index (III). The III for MLC was defined as

$$\frac{\text{c.p.m. in mixed cultures}}{\text{c.p.m. in unmixed cultures} \div 2}$$

and for PHA cultures as

$$\frac{\text{c.p.m. in cultures with PHA}}{\text{c.p.m. in cultures without PHA}}$$

Cytotoxicity assays were performed in 6 mm × 50 mm tubes. To each tube was added 50 µl. of a suspension of spleen cells labelled with ^{51}Cr (5×10^4 cells) and 50 µl. of either medium or test sera. The sera used included tetraparental, mixed parental, F_1 hybrid or monospecific anti H2 sera (C–2, C–19, C–33, obtained through the Transplantation Branch, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland). The tubes were incubated at room temperature for 15 min and 50 µl. of a 1 : 10 dilution of rabbit serum was added as a source of complement. The tubes were centrifuged 45 min later and the release of ^{51}Cr determined and compared with that released from cells exposed to complement alone and from cells frozen and thawed four times. The maximum percentage of releasable ^{51}Cr by each antiserum was calculated as:

$$\frac{^{51}\text{Cr released by cells exposed to antiserum} - {}^{51}\text{Cr released by cells in medium}}{^{51}\text{Cr released by frozen and thawed cells} - {}^{51}\text{Cr released by cells in medium}} \times 100\%$$

Table 1 Effect of Tetraparental Mouse Serum on Proliferative Response of Parental Strain Cells to PHA

Mouse strain	Serum	Isotope incorporation index	Significance level
SJL	—	28.5 ± 2.1	
	Tetraparental	22.7 ± 3.1	NS
	Mixed parental	21.9 ± 3.4	NS
	F_1 hybrid	27.9 ± 1.9	NS
C57Bl/10	—	37.1 ± 3.5	
	Tetraparental	34.1 ± 3.6	NS
	F_1 hybrid	39.2 ± 2.51	NS

Serum concentration was 1 : 20; the mean ±s.e. for four determinations is given. NS, Not significantly different from response in absence of added serum ($P > 0.05$).

Table 2 Effect of Tetraparental Mouse Serum on One Way MLC involving Parental (C57Bl/10 and SJL) and Third Party (CBA and BALB/c) Strain Cells

Responding cell	Target cell*	Isotope incorporation index† No serum	F_1 hybrid[3]	Tetraparental serum‡	Significance level, *P*§
C57Bl/10	CBA_m	12.1 ± 1.6	14.5 ± 1.6	13.4 ± 1.9	NS
SJL	$BALB/c_m$	6.9 ± 0.9	7.3 ± 1.1	6.6 ± 1.3	NS
CBA	$C57Bl/10_m$	5.6 ± 0.6	6.2 ± 0.8	2.3 ± 0.3	<0.001
BALB/c	SJL_m	6.7 ± 1.2	6.4 ± 0.9	2.1 ± 1.1	<0.07

* Target cells were rendered non-responsive by mitomycin (m) pretreatment.

† Mean ±s.e. of three determinations.

‡ Serum concentration was 1 : 20.

§ Comparison between control response in absence of added serum and response in presence of tetraparental serum.

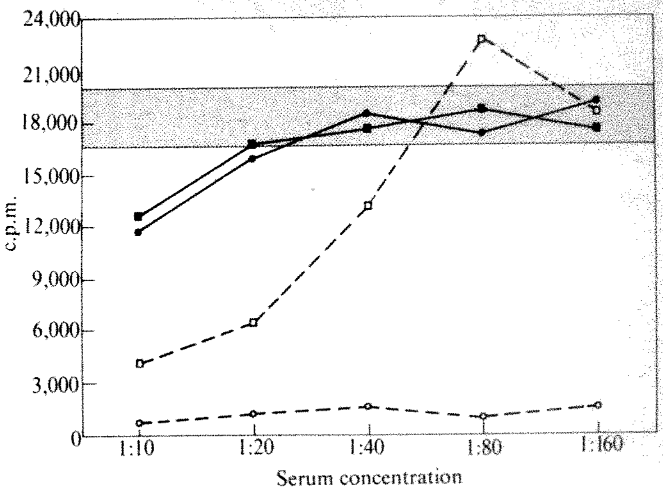

Fig. 1 Effect of tetraparental mouse serum on the incorporation of ^3H-thymidine by MLC between parental strain cells. The shaded area represents the 95% confidence limits of ^3H-thymidine incorporation in MLC in the absence of mouse serum. The incorporation of ^3H-thymidine for control cells was taken as the mean incorporation of the two parental cells cultured separately. Each point represents the mean of four determinations. The average standard error of the mean was less than 10%. ○, Control cells; ●, normal F_1 serum; □, tetraparental serum; ■, mixed parental serum (1 : 1 V/V).

The effect of tetraparental serum on the immunological interaction of parental strain cells was investigated. MLCs between C57Bl/10 and SJL cells were incubated in the presence and absence of tetraparental sera. Control cultures contained either a 1 : 1 mixture of parental sera or F_1 hybrid serum. Tetraparental serum at concentrations of 1 : 40 and higher significantly inhibited the MLC between parental cells (Fig. 1). At a concentration of 1 : 80 a small but significant stimulation was found. Control sera, except at the highest concentration tested (1 : 10), were without suppressive effect. The results depicted in Fig. 1 were obtained using a pool of sera obtained from seven tetraparental animals. Individual sera showed varying amounts of blocking activity.

The specificity of the inhibitory effect of tetraparental sera was determined in two ways. First, the response of parental strain cells to PHA was measured in the presence and absence of a concentration of tetraparental serum previously shown to inhibit the MLCs between parental strain cells. Tetraparental serum was without effect on this response (Table 1). Second, one way MLCs were established between parental strain (C57Bl/10 or SJL) and third party strain cells (BALB/c or CBA) (Table 2). Tetraparental serum did not inhibit the response of parental strain cells against mitomycin-treated third party target cells. Tetraparental sera, but not mixed parental or F_1 hybrid sera, did, however, significantly reduce the response of third party cells against mitomycin-treated parental strain cells.

Preliminary observations suggested that the blocking factor is directed against H2 antigens because cells differing from parental strain cells only at the H2 locus could not be blocked in the one-way MLC reaction (manuscript in preparation).

Tetraparental sera were therefore checked for direct cytotoxicity against parental strain cells in the presence of complement and also for their ability to block monospecific cytotoxic sera directed against H2 specificities present on parental cells (Table 3). The use of congenic strains in appropriate one-way MLCs has further shown that the serum blocking factor has specificity for the allelic products of the H2 locus (manuscript in preparation). Tetraparental sera were not cytotoxic to parental strain cells. Further, preincubation of anti-H2 sera or prior exposure of target cells to tetraparental serum did not significantly reduce antibody-induced lysis.

Preliminary studies suggest that the blocking factor may be an immunoglobulin; it is insoluble in 35% saturated ammonium sulphate and can be removed from serum by the formation of precipitate with goat anti-mouse immunoglobulin serum.

Table 3 Effect of Tetraparental Mouse Serum on Cytotoxic Activity of Monospecific Anti-H2 Sera

Specificity of anti-H2 serum	Per cent ±s.e. maximum ^{51}Cr release Control	Anti-H2 serum preincubated with tetraparental serum	^{51}Cr-labelled cells preincubated with tetraparental serum
C-2	46.3 ± 3.2	48.6 ± 1.9	41.8 ± 2.3
C-33	56.3 ± 4.5	57.2 ± 2.9	47.5 ± 2.9
C-19	73.5 ± 4.9	67.0 ± 2.0	69.9 ± 3.7

Anti-H sera C-2 and C-33 detect specificities present on C57Bl/10 cells, while serum C-19 detects specificity on SJL cells. The antisera were tested on the appropriate target cell at a concentration of 1 : 100. A 1 : 50 dilution of anti-H2 sera was preincubated at room temperature for 60 min with an equal volume of a 1 : 30 dilution of tetraparental mouse serum.

^{51}Cr-labelled target cells were exposed to a 1 : 30 dilution of tetraparental serum for 30 min at room temperature, before the addition of anti-H2 sera. Tetraparental serum was shown to have no direct cytotoxic effect on ^{51}Cr-labelled target cells.

To determine whether the serum factor blocked spontaneous autoreactivity in tetraparental spleen cells, spleen cells from individual tetraparental, parental or F_1 hybrid mice were cultured in the presence of tetraparental, mixed parental, or F_1 hybrid sera (Table 4). Isotope incorporation was determined after 72 h. Tetraparental serum significantly reduced the level of blastogenesis by tetraparental cells but did not affect that of parental or F_1 hybrid cells. Control sera, F_1 hybrid and mixed parental, did not significantly suppress isotope incorporation by either tetraparental, parental or F_1 hybrid spleen cells.

Our results demonstrate the existence of a serum factor in tetraparental mice capable of blocking immune interaction between parental strain cells. In view of these and the earlier

Table 4 Effect of Tetraparental Mouse Serum on Spontaneous Blastogenesis of Tetraparental Mouse Spleen Cells

Animal	Radioactivity incorporated (c.p.m.)* No tetraparental mouse serum	Radioactivity incorporated (c.p.m.)* 1 : 20 tetraparental mouse serum	Reduction (%) due to tetraparental mouse serum
Parental	1,007 ± 172	942 ± 151	5.5
F_1 hybrid	1,994 ± 307	1,884 ± 376	5.5
Tetraparental	3,472 ± 451	1,612 ± 198	53.6

Mixed parental and F_1 hybrid sera had no suppressive effect on the spontaneous blastogenesis of parental, F_1 hybrid, or tetraparental mouse spleen cells.

* Mean ± s.e. of four determinations.

results of a microcytotoxicity assay, it seems that immunological non-reactivity between the allogeneic cells of a tetraparental mouse is achieved, not by the elimination of self-reactive immunocytes, but by serum-mediated suppression of self-reactivity. Whether serum-mediated tolerance to self-antigens is also found in normal animals remains to be established. The absence of a factor in F_1 hybrid serum capable of suppressing MLCs between parental strain cells suggests that lack of autoreactivity against the principal H2 antigens in normal biparental animals is not serum-mediated. An immunocyte with antibody reactive with antigen present in the same cell might be destroyed; but where the immunocyte antibody is directed against self-components not present on the lymphocyte, this potential reactivity could be blocked by serum factors. Cohen *et al.*[12] showed that inbred rat lymphocytes preincubated with isogeneic fibroblasts *in vitro* could destroy a second set of such fibroblasts *in vitro*, as well as mediate a mild graft versus host reaction if given to newborn rats of the same strain. It therefore seems that the normal rat contains cells capable of recognizing antigens present on the animal's fibroblasts. It would be interesting to know whether the sensitization *in vitro* would still occur in the presence of autologous serum. The mechanism whereby serum factor blocks the MLC is unknown, and experiments are under way to test the various possibilities.

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Effect of Ethylene on Root Extension of Cereals

THE extension of root axes of barley is severely inhibited by concentrations of ethylene considerably lower than those which can occur in anaerobic soil[1]; the sensitivity of this species has now been compared with that of three other temperate cereals and several varieties of rice from Nigeria, together with two dicotyledonous plants known to be particularly susceptible to injury from anaerobic soil conditions.

Young plants, with root axes about 10 cm long, were sealed through the gas-tight lids of 1,600 ml. cylindrical jars, with their roots in contact with filter paper which dipped into culture solutions in the bottom of the jars. The work was carried out in a controlled environment with a day length of 16 h and a light intensity of 18–20,000 lux; the temperature was maintained constant at 20° C for all species except rice, for which day and night temperatures were 25° C and 20° C respectively. After the roots had been in contact with the filter paper for 24 h, various concentrations of ethylene were applied; root extension was measured over the next 3 days, the concentrations of ethylene being monitored daily by gas chromatography[1].

The sensitivity of different species varied very widely (Table 1). Barley was the most sensitive of the temperate cereals and rye the least; some rice varieties were considerably more resistant than any temperate cereal. In Fig. 1 response curves for barley, rye and the most resistant rice variety (OS6) are compared. Concentrations of ethylene below 1 p.p.m. caused small increases in root extension in both rice and rye; a significant reduction (about 25% in rice and 40% in rye) occurred when the concentration was increased to about 10 p.p.m., but the magnitude of the effect was not increased by considerably higher concentrations (up to 350 p.p.m. with rice). In contrast, root extension in barley was not stimulated even at the lowest

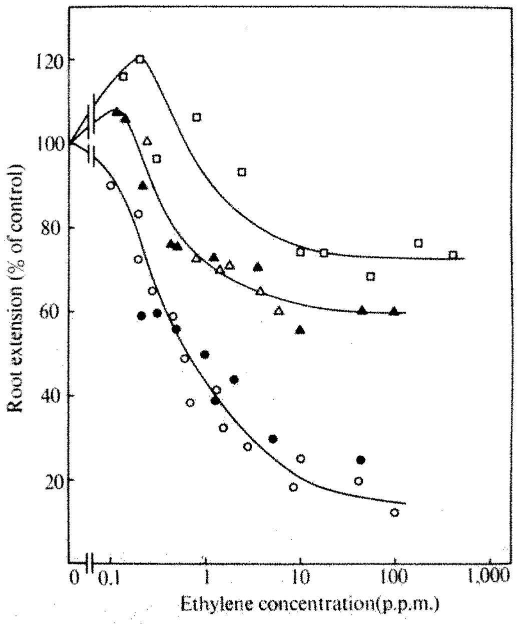

Fig. 1 The effect of ethylene on the extension of root axes of barley, rye and upland rice. Roots were exposed to ethylene for 3 days. □, Rice, OS6; ▲, rye, Ovari; △, rye, Lovasz Patonai; ●, barley, Proctor; ○, barley, Maris Badger.

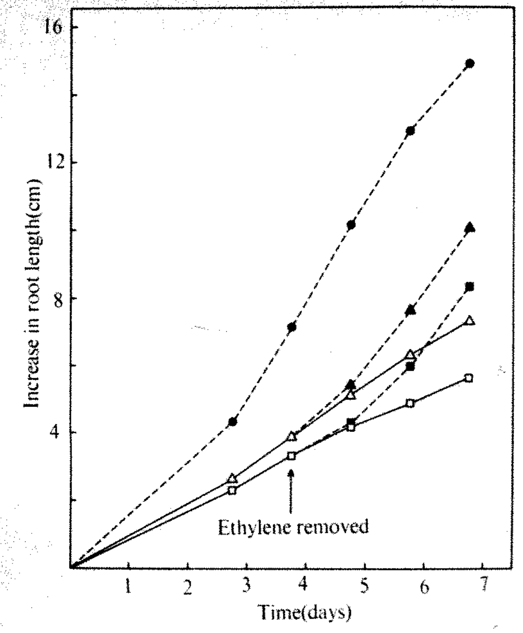

Fig. 2 Recovery of extension rate of barley roots after 4 days' exposure to sub-lethal concentrations of ethylene. Roots exposed to: ▲, 0.2 p.p.m. ethylene for 4 days; △, 0.2 p.p.m. continuously; ■, 1.2 p.p.m. for 4 days; □, 1.2 p.p.m. continuously; ●, control.

levels of ethylene, and 10 p.p.m. caused root extension to cease by the end of a 3 day period, a profusion of root hairs developing within 1–2 mm of the swollen apices. No anatomical abnormalities were observed at low concentrations which caused root extension to decrease by not more than about 50%; when ethylene was removed the normal rate of root elongation was then resumed within 1–2 days (Fig. 2). Although barley is more sensitive than any other cereal which has been examined, tomato and tobacco are still more affected, root extension being reduced to about one-quarter of the normal rate by 1 p.p.m. of ethylene.

Table 1 Effects of Ethylene on Root Extension of Cereals after Exposure for 3 Days

Species	Root extension (% of control) 1 p.p.m.	20 p.p.m.
Temperate cereals		
Barley (Maris Badger and Proctor)	45	20
Oats (Condor)	55	20
Wheat (Maris Widgeon)	70	60
Rye (Lovasz Patonai and Ovari)	75*	60
Rice		
SML 140/10	55	25
Mas 2401	75	50
BG 79	85	55
Mali Ong	75	50
Agbede	90*	75
OS6	100*	75

* >100% of control at 0.1–1 p.p.m.

No explanation is available for these interspecific differences but there is other evidence of the unusual response of rice to ethylene[2]. Variations in the concentration of carbon dioxide up to levels which themselves reduce root extension do not affect the response of roots to ethylene. It has been observed that when barley seed has been stored in conditions which cause the percentage germination to decrease, the plants grown from the seeds which do germinate show an appreciably increased tolerance to ethylene.

Attention has recently been directed[3] to the reduction in crop yields which results from inadequate drainage, and hence anaerobic conditions, in heavy soils in many parts of the United Kingdom. It is therefore interesting that concentrations of ethylene capable of causing appreciable injury to temperate cereals can occur, apparently through microbial activity, when a wide range of soils are maintained in anaerobic conditions[4]. The view that ethylene deserves consideration among the causes of waterlogging injury is further encouraged by the fact that the temperate cereals fall into approximately the same order with respect to their tolerance to ethylene as to their survival of waterlogging under field conditions.

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Use of a Sustained-release Multiple Emulsion to Extend the Period of Radioprotection conferred by Cysteamine

Practical application of the substances which protect biological systems against ionizing radiation has been limited by their toxicity and because they are often metabolized so rapidly that they give protection only for a short time[2]. We have incorporated the protective chemical cysteamine (mercaptoethylamine, MEA) in a sustained-release multiple emulsion[3] in an attempt to extend the duration of protection in mice.

Cysteamine was injected intraperitoneally into female CS1 specific pathogen-free mice which were then irradiated at various times with 250 kVp X-rays filtered through 0.5 mm copper and 0.5 mm aluminium and delivered at a dose rate of 200 rad/min. Seven days later 1μCi ^{59}Fe was injected intraperitoneally, and 3 days later the mice were killed. Blood was withdrawn from the heart and its ^{59}Fe content was measured to estimate total body erythropoiesis[4]; the spleen was weighed and fixed in Bouin's solution to render surface colonies (derived from haematopoietic stem cells) visible[5]. After doses of 350–500 rad, and in highly protected mice, colonies became confluent and therefore uncountable; the fraction of spleens producing confluent colonies was therefore used as the measure of colony formation.

Cysteamine was administered at a dose of 120 mg/kg body weight in aqueous solution, or at a dose of 340–400 mg/kg body weight when in the emulsion[3] (formulated according to National Research Development Corporation patents 33255/67, 25146/68 and 56421/69). An 8% solution of cysteamine was slowly added to an equal volume of light liquid paraffin containing 10% of the detergent 'Arlacel 83' (sorbitan sesquioleate) and homogenized in a Silverson blender. This was added to an equal volume of a 2% aqueous solution of 'Tween 80' (Honeywill Atlas Ltd) and shaken by hand to form the final multiple emulsion. The final stage of the emulsion had to be prepared within 30 min of administration; with longer intervals larger numbers of mice died because the emulsion degrades with time causing a more immediate release of cysteamine after injection, killing the mice. It is now possible, however, to prepare a more stable emulsion using 'Squalene' (BDH) and 'Arlacel A' instead of light liquid paraffin and 'Arlacel 83'.

We have compared radiation responses in irradiated mice protected by cysteamine with the responses in unprotected mice receiving 350 to 700 rad; this enables dose reduction factors to be estimated for the protected mice. If x rad produces the same

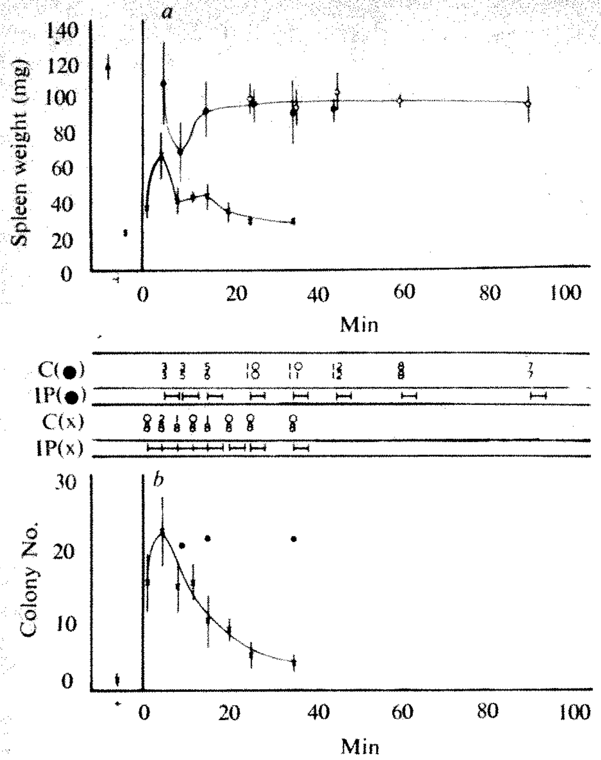

Fig. 1 Effect of cysteamine administered at various times before or after irradiation on mouse spleen weight and the number of visible colonies on the surface of mouse spleen 10 days after 700 rad total body irradiation. *a*, Spleen weight; *b*, spleen colony number, and fraction of spleens totally confluent at each irradiation time. Cysteamine in water, ×. Cysteamine in emulsion, ●. Sham irradiated controls, ▲. Cysteamine given after irradiation, +. C, Fraction of spleens totally confluent. IP, Irradiated period (3.5 min).

effect in protected mice as y produces in unprotected mice, then the dose reduction factor given by the protector is x/y. The parameters studied, which were spleen weight, colony counts and the percentage of spleens showing confluence, decreased progressively with increasing radiation dose in the range 350 to 700 rads.

When cysteamine was administered in aqueous solution, protection was maximum when it was given 7–10 min before 700 rad of total body irradiation, but had decreased to nearly zero when there was an interval of 20 min between injection and irradiation (Fig. 1). Thus significant protection is only given when irradiation takes place between 5 and 15 min after administration of the chemical, which is in accordance with previous findings. The dose reduction factors for the parameters examined did not exceed 1.7: even when the dose of protector was nearly lethal the dose reduction factor did not exceed 1.8 to 1.9.

When cysteamine was administered in an emulsion there was again a rapid increase in radioprotection during the first few minutes after injection (Fig. 1). This protection did not, however, decrease during the following 15 min; in contrast, it increased further and remained high for at least 1.5 h. In addition, the dose reduction factors estimated for the parameters spleen weight and colony count were significantly higher than those obtained when the cysteamine was administered in aqueous solution, for dose reduction factors greater than 2 were found up to 1.5 h after injection. Since all spleen colonies are confluent after doses of less than 500 rad, or in heavily protected mice, it was necessary to use a percentage of spleens that were totally confluent to estimate the dose reduction factor; this allows the estimation of dose reduction factors up to 2. Even using this system, however, it was only possible to define the dose reduction factor as being greater than two.

Uptake of ^{59}Fe into red cells was measured in some mice to give an estimate of total body erythropoiesis. Here again cysteamine incorporated in an emulsion conferred a high level of protection which was maintained over the period studied.

Mortality experiments were insufficiently precise for dose reduction factors to be estimated. It was clear, however, that considerable and prolonged protection against the lethal effects of X-irradiation also occurred, even when that irradiation took place 90 min after administration of the protector, since there was very little mortality in any of the protected groups (less than 15%), compared with 85% mortality in non-protected mice.

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New Method of Locomotion in Limbless Terrestrial Vertebrates

Four main types of locomotion have been described in limbless terrestrial vertebrates[1,2]. Three of these (serpentine, concertina and sidewinding) depend on lateral undulations which are essentially similar to those of aquatic vertebrates, although more complex. The fourth, rectilinear locomotion, is found in some limbless animals which need to move in conditions which prohibit lateral undulations. The skin in these animals is largely free from the underlying muscles for part or all of the body circumference, being attached only by specially developed cutaneous muscles. These move the skin in segmental units and also transmit the locomotor forces to the body, which is driven forwards continuously while the skin is regionally engaged in static friction with the substrate. The spinal column and ribs remain straight. In amphisbaenids, in which rectilinear locomotion is best developed[3], the external appearance resembles that of an earthworm. The skin folds between annular regions of attachment to produce thickened regions which pass along the body.

The limbless amphibians (caecilians, Apoda or Gymnophiona) look even more like earthworms. The skin, musculature and many of the internal organs are segmentally organized. Like amphisbaenids they are able to move by worm-like regional contractions as well as by lateral undulations. The taxonomy of these animals has only recently received detailed attention[4]. Most of the 155 species described seem to be carnivorous burrowing animals, which are distributed throughout the tropics (excepting Australia). They seem especially successful at medium altitudes, where they are usually found in moist, humic soil, often near water. The remaining twenty or so species form an aquatic family (Typhlonectidae) confined to South America.

The mechanisms of movement in caecilians have apparently been ignored since they were thought to lack locomotor specializations[1]. A study of *Hypogeophis* has demonstrated that, far from being unspecialized, this amphibian is able to move by a unique method which makes widespread anatomical demands,

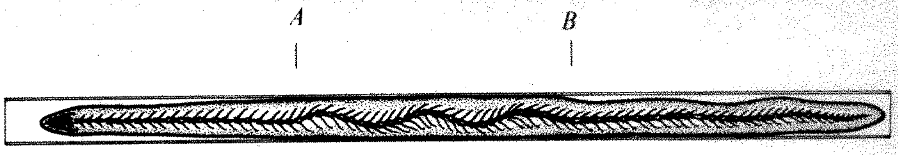

Fig. 1 The caecilian *Hypogeophis* moving through a plastic tube. The contracted region *A–B* is moving backwards relative to the head. Drawn from an X-ray photograph. (×0.5.)

providing an explanation for many of the unique features common to this fossorial group.

Live specimens of *Hypogeophis* collected in the Seychelles were observed while moving in restricted conditions (in a tube or channel) using cine X-ray apparatus. Single X-ray photographs were also taken, of both live and dead specimens, and the behaviour of live animals was observed in laboratory conditions. The skeletal and muscular anatomy of *Hypogeophis* was investigated in the light of the locomotor performance, using dissections and serial sections. H. P. Whiting (personal communication) has observed in an X-ray photograph of a museum specimen of *Ichthyophis* that the spine is folded within the body outline. Published X-ray photographs confirm that this is often the case in fixed specimens of many other genera[4], and X-ray photographs of *Hypogeophis* show that the same may be true in living caecilians (Fig. 1).

The implications are clear: the shortened, thickened regions visible externally during worm-like movements correspond to spinal flexion, rather than solely to skin contraction as in rectilinear locomotion.

The annuli in the shortened regions grip the sides of the tube or tunnel, providing resistance against which the head is pushed forwards as the spine straightens. The tail region is pulled forwards as new wave-forms are developed, the thickened region containing spinal folds passing rapidly backwards relative to the head. Two such contracted regions may be present at the same time.

The result is very worm-like, the spine replacing the hydrostatic skeleton, but the skin and body-wall muscles performing in much the same way as in worms, and with a similar annular organization. This movement will therefore be termed vermiform locomotion.

This method of locomotion has special advantages to a burrowing animal. As in rectilinear locomotion, lateral flexions of the body are not necessary, which permits movements in tunnels in which most limbless tetrapods would be helpless. Vermiform locomotion has the advantage over rectilinear that more power can be produced, since large regions of the massive spinal musculature are involved rather than merely thin bands of cutaneous muscles. *Hypogeophis* is able to ram through soft earth by vermiform locomotion when unable to "swim" through by lateral undulations. Amphisbaenids probably use rectilinear locomotion chiefly for passing through tunnels previously dug by head movements[3].

The evolution of vermiform locomotion was probably accompanied by increased internal stresses caused by the mobile spine and surrounding muscle, and the regional contractions and expansions of the body. The anatomy seems much modified to meet these demands. This will be discussed in detail later, but the essential modifications in muscular arrangement can be clearly seen in transverse sections (Fig. 2).

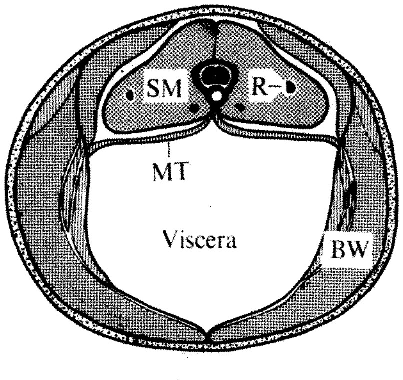

Fig. 2 Diagrammatic transverse section through the mid-body region of *Hypogeophis*. SM, Spinal muscle; R, rib; MT, transversus muscle; BW, body-wall muscles.

The segmental body-wall muscles are closely bound to the skin, the myosepta being continuous with the inner dermal connective layers. To move laterally within the body wall, the spinal muscle is free of attachment except at the skull and tail, and by a thin sheet of muscle (m. transversus) and connective fibres running from the mid-line ventro-laterally on each side. This sheet is able to transmit the forces between the skin, engaged with the tunnel wall, and the spinal column. The only other connexions are provided by looped spinal nerves and blood vessels, which are well able to accommodate the movement of the spinal muscle relative to the body wall without risk of rupture.

The ribs are firmly bound to the vertebrae, but they can move in a plane joining the dorsal and ventral articulations. As the spine is pressed laterally against the body-wall muscles the spinal muscle distorts, extending downwards, and the rib on that side is pressed downwards and backwards nearer the spine.

Although the ribs are larger in caecilians than in other living amphibians it is clear that vermiform locomotion could not have developed had the ribs originally extended into the body-wall muscle close to the skin, as in reptiles. Reptiles were thus prevented from developing this locomotory method by their use of the ribs in respiratory movements.

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Threshold Levels for Damage of the Cornea following Irradiation by a Continuous Wave Carbon Dioxide (10.6 μm) Laser

CORNEAL damage of varying severity has been studied in the rabbit (*Cuniculus oryctolagus*) and monkey (*Macaca mulatta*) following exposure to a continuous wave carbon dioxide (10.6 μm) laser. The laser consisted of a 1.5 m glass tube with a water cooled jacket. The tube contained a mixture of carbon dioxide (partial pressure 0.64 mm Hg), nitrogen (partial pressure 1.28 mm Hg) and helium (partial pressure 6.08 mm Hg). A curved stainless steel mirror and an Irtran plain mirror, with a 0.3 cm diameter window, formed a hemispherical cavity. The tube was excited by a 10 kV d.c. supply capable of delivering 100 mA. The mirrors were adjusted to give a TEM$_{00}$ mode pattern. The emergent beam, which had a divergence of 4 m radians measured between 1/e points, was directed through a limiting aperture of approximately 0.2 cm diameter and finally through an aperture of 0.25 cm diameter placed directly in front of the eye. The distance between the apertures determined the incident corneal power density. The power distribution of the beam emitted by the laser was Gaussian and beyond the final aperture it was approximately rectangular, that is at a distance of 1 m the edges were limited to 88% of the centre of the Gaussian curve. The total power output of the laser was 20 W.

In each animal an area of about 0.05 cm^2 (0.25 cm diameter) was irradiated for 70 ms. The exposure was carried out during pentobarbitone sodium anaesthesia (30 mg/kg intravenously).

Three grades of corneal damage were recognized. Grade I, which could be observed but not photographed by slit lamp microscopy, was a very faint opalescence of the epithelium. These lesions resolved within 24 h in the rabbit and within 48 h in the monkey. A grade II lesion involved epithelial loss, which persisted beyond the duration of a grade I lesion, but healed completely within 7 days, and a grade III lesion involved coagulation of the substantia propria with scarring of the cornea.

In ninety-eight pigmented rabbits, weighing between 1.5 and 3.2 kg (mean weight, 2.1 kg), 629 exposures were made with corneal incident power densities ranging from 2.5 to 35.7 W cm^{-2}. In this species the presence of the precorneal film was ensured by irrigation of the eye with normal saline 45 s before exposure. The 50% probabilities of damage were 5.8 W cm^{-2} for grade I, 9.7 W cm^{-2} for grade II and 17.4 W cm^{-2} for grade III. The lowest power density which led to reversible damage (grade I) was 4.0 W cm^{-2} and to irreversible damage (grade III) was 8.0 W cm^{-2}.

In six monkeys, weighing between 4.0 and 5.2 kg (mean weight, 4.7 kg), eighty-eight exposures were made with corneal incident power densities ranging from 2.0 to 21.0 W cm^{-2}. Probability analyses were not applicable to this more limited series but the lowest power density which led to reversible damage (grade I) was 6.9 W cm^{-2}.

Vassiliadis *et al.*[1] reported that the 50% probability of minimal damage in the rabbit was 22.0 W cm^{-2} and in their studies the lowest power density which produced damage appeared to be about 21 W cm^{-2}. We consider that many factors may be responsible for the differences between these and our results. We have used a very faint opalescence as the criterion for minimal (grade I) damage but Vassiliadis *et al.*[1] did not use such a small change in corneal structure as their lesions could be recorded easily by slit lamp photography.

There are also differences in experimental techniques. Vassiliadis *et al.*[1] defined corneal power density as the total power contained in the beam divided by the area contained by the 1/e point of the Gaussian beam distribution, whereas in our studies it was defined as the total power passing through the aperture in front of the cornea divided by the area of the aperture. A difference of 25% in the stated figure for power density could result from identical exposures using these two methods of expressing power density. Further, in their study[1] change in power density was accompanied by change in the area of cornea irradiated and the influence of area irradiated on thresholds for damage has not been established. This is a factor which needs consideration. Their techniques of measurement are not feasible if the irradiated area is to remain constant and the results could suggest, to the unwary, a higher power density than necessary to produce minimal injury. It must also be borne in mind that Vassiliadis *et al.*[1] used an exposure duration of 55 ms and calculations on their data suggest that for an exposure of 70 ms the 50% probability of minimal damage would be reduced to 18.0 W cm^{-2}.

Although the primate cornea is almost certainly less sensitive to 10.6 µm irradiation than the rabbit we consider that data obtained from the rabbit should continue to be used for safety considerations in man, at least until more experience is gained. We recommend that the derivation of hazard levels for continuous wave carbon dioxide (10.6 µm) lasers should now be based, for most purposes, on the lowest power which we have observed to produce minimal corneal damage within 70 ms, that is 4.0 W cm^{-2}. It must be emphasized that we have observed corneal scarring in 13 rabbits within a power density range from 8.0 to 14.0 W cm^{-2}.

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Comparative Psychotomimetic Effects of Stereoisomers of Amphetamine

GRIFFITH's demonstration in 1968 that amphetamine psychosis could be induced safely in non-psychotic human subjects made it feasible to study this psychosis in controlled experimental conditions[1], and later the clinical symptoms induced by large doses of amphetamine were identified[2,3]. There were also attempts to investigate pathogenic factors in this condition, using pharmacological pretreatments which affected biogenic amines, and observing the effects on behavioural responses to amphetamine[3,4]. Another approach to the study of possible pathogenic factors was suggested by recent reports[5,6] of differential biochemical and behavioural effects of *d* and *l*-amphetamine. The essence of these findings is that the *d* form of amphetamine was found to be ten times as potent as the *l* form in inhibiting accumulation of noradrenaline in synaptosomes from noradrenergic brain areas, while the two forms were equipotent in their effects on the accumulation of dopamine in synaptosomes from the striatum. Behavioural correlates in rats indicated a similar 10 to 1 potency for *d* against *l*-amphetamine for the induction of motor hyperactivity. The *d* isomer, however, proved only one to two times as potent as the *l* form in inducing stereotyped behaviour in rats. This suggested that the motor activity induced by amphetamine was noradrenergically mediated. The results with regard to stereotypy, however, suggested that dopaminergic, or other non-stereospecific mechanisms, were largely involved in the induction of behavioural stereotypy, but that noradrenergic mechanisms might also contribute since the potency of *d* to *l*-amphetamine was found to be between 1 and 2 to 1, not 1 to 1 as might be expected if only non-stereospecific mechanisms were involved. Moreover, these findings were consistent with biochemical and neuroanatomical studies[7-10] which suggested a critical role for dopaminergic mechanisms in the induction of behavioural stereotypies.

We therefore reasoned as follows. Psychosis can, of course, only be studied in humans. Snyder's data[6], however, suggested that the differential behavioural response of subjects to *d* and *l*-amphetamine might provide clues to psychotogenic mechanisms. If noradrenergic mechanisms and behaviourally correlated motor stimulation were critical in psychotogenesis then one might expect *d*-amphetamine to have ten times the potency of the *l* form in inducing psychosis as a behavioural effect. Similarly, if dopaminergic mechanisms only were involved, then one might expect the two compounds to be equipotent in causing a psychosis. If animal stereotypy is a valid model for the stimulant psychoses in humans, then a potency for *d* against *l*-amphetamine of the order of between 1 and 2 to 1 might be anticipated.

We conducted our experiment as described in detail previously[3]. Basically, it is similar to the methodology developed by Griffith[2], but involves somewhat larger individual doses. Amphetamine is administered orally, and 1 h later pulse, blood pressure and temperature are taken. The next dose was determined on the basis of the stability of these signs. The maximum hourly dose used was 50 mg, but smaller doses were administered when effects on pulse, blood pressure and temperature were noted. Amphetamine was administered hourly around the clock with a physician in constant attendance. Behavioural effects were identified by psychiatric interviews every 2 to 3 h. Two interviews each day were videotaped. Racemic amphetamine was given before experiments with the *d* and *l* isomers to establish approximate thresholds for behavioural effects in each subject.

Table 1 Stereoisomeric Form, Cumulative Dose, Duration of Administration and Behavioural Response of Subjects to the Administration of Amphetamine in Large Doses

Patient No.	Type of amphetamine used	Cumulative dose (mg)	Time (h)	Behavioural response (0–6)
1	*d, l*	540	30.0	4
	d	510	26.25*	4
	l	640	30.0	5
2	*d, l*	465	22.75	6
	d	270	17.25	5
	l	415	22.50	4
3	*d, l*	400	24.5	3
	d	475	25.0	3
	l	475	21.25	3

* Tachycardia necessitated discontinuation of experiment.

The stereoisomeric forms of amphetamine, cumulative doses, and the time for which amphetamine was administered are indicated in Table 1; the numbers in the last column refer to the intensity of the psychosis induced, scored from 0 to 6. The qualitative aspects of these responses will be described in detail later.

The intensity of symptomatology and dose-response relationships do not support the idea that noradrenergic mechanisms are critical in precipitating amphetamine psychosis. Certainly, the psychotogenic potency was nowhere of the order of 10 to 1 for the *d* against the *l* isomer. If just the *d* and *l* experiments are considered, subject 1 showed approximately the same degree of symptomatology at doses of 510 and 640 mg of *d* and *l*-amphetamine, respectively. Subject 2 showed slightly more severe symptoms after 270 mg of *d*-amphetamine than after 415 mg of the *l* isomer, while the third subject showed a similar behavioural response after the same dose of the *d* and *l* isomers. In other words, the mean dose of *d*-amphetamine given to these three subjects was 418 mg and that of the *l* isomer was 510 mg—both induced comparable syndromes in the three subjects and equal mean scores of behavioural disturbance of 5 (on a scale of 0–6). This suggests that noradrenergic mechanisms are not the most critically important factor in amphetamine psychosis, and further studies should be focused on the role of dopaminergic or other non-stereospecific mechanisms. Moreover, the fact that dose-response relationships indicate a psychotogenic potency for the *d* and *l* isomers of amphetamine of the order of between 1 and 2 to 1 suggests that animal stereotypy, in which dose-response relationships are of the same order[5,6,11], should be utilized as an animal model for the human stimulant psychoses. The established role of dopaminergic mechanisms in the induction of these behavioural stereotypies[7–9] suggests that the role of these mechanisms in the pathogenesis of the human stimulant psychoses should be investigated. Further support for this orientation comes from the observation of psychotic symptoms in Parkinsonian patients receiving L-dopa[12] (which increases brain dopamine more consistently than noradrenaline[13]), and from the demonstrated capacity for L-dopa to induce stereotypy in rats[14], cats[15] and dogs[10].

The striking clinical similarity of amphetamine psychosis to paranoid schizophrenia[16], moreover, suggests that these conditions might have common mechanisms. The fact that drugs which antagonize amphetamine stereotypy in animals also tend both to be useful neuroleptics in the treatment of schizophrenia and, in addition, cause a Parkinsonian syndrome in humans also suggests that subsequent investigators focus on the role of dopaminergic mechanisms in naturally occurring psychoses—especially those in which paranoid symptoms are prominent.

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Reaction of Metallic Copper with Biological Substrates

IT has been shown by Zipper *et al.*[1] that a plastic T-shaped intrauterine device is much more effective in preventing pregnancies in women if its stem is encased by copper wire. After removal of the copper intrauterine device from the human uterus, the copper wire is blackish and weighs less than at the time of insertion; a device with a 200 cm^2 copper surface loses 60 μg per day of usage (personal communication from H. J. Tatum).

This loss of metallic copper has prompted me to investigate the interaction of metallic copper with various biological substrates. In all experiments electrolytic grade copper foil of various dimensions was placed in solutions of substrates incubated at 37.5° C. After various times of incubation the solutions were analysed for cupric ions with the diethyl ammonium salt of diethyl dithiocarbamic acid, which forms a yellow chelate with cupric ions.

A copper strip with a surface area of 400 mm^2 was placed in a mixture of approximately 0.5 ml. of human uterine secretion and 2 ml. of physiological saline (0.9%). The uterine secretion was initially a thick clear mucoid material. After 18 h of incubation this material was lysed, and no longer viscous; a precipitate had formed and the copper strip was blackened. The Cu^{2+} concentration in the solution was 1.8×10^{-3} M. An 18 h incubation of a copper strip in 2.5 ml. of saline solution alone yielded a Cu^{2+} concentration of 4×10^{-5} M. Because uterine secretions are slightly alkaline, a copper strip was incubated for 18 h in *p*H 8 carbonate buffer, but the corrosive action was slight as with saline. Uterine secretion incubated with saline but without the metallic copper still showed a coherent mucoid mass after 18 h of incubation. The amount of copper dissolved by the uterine secretion, calculated for a 200 mm² Cu surface, amounts to 60 µg per day, if one assumes 1 ml. of secretions per day, agreeing well with the clinical data.

An 18 h incubation of 1.8 ml. of human ovulatory cervical mucus (without added saline) with a copper strip (400 mm² total surface) showed a lysis of the mucoid material and a Cu^{2+} concentration of 1.0×10^{-2} M. The copper-incubated cervical mucus was brought into contact with washed sperm, which was inactivated within 2 h of incubation at 37.5° C; in a parallel experiment with normal cervical mucus there was no comparable inactivation.

To elucidate the mechanism of the dissolution of metallic copper, bovine serum albumin was used as a model substrate, since the interaction of serum albumin and mucins gives cervical mucus its cohesiveness. Bovine serum albumin dissolved in water showed a dissolution of metallic copper which was proportional to the time of incubation (measured up to 24 h) and to the surface area of the copper strip (80–720 mm²). Fig. 1 shows that the rate of dissolution of copper increases both with increasing salt and serum albumin concentrations. During this dissolution process protein is precipitated. The turbidity as a function of albumin concentration (Fig. 2) had a pronounced maximum.

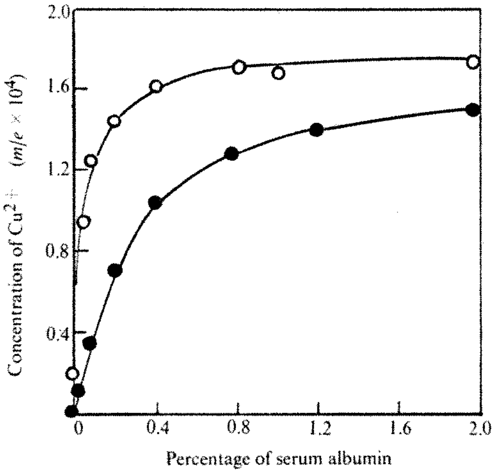

Fig. 1 Cupric ion concentration in serum albumin solution after 90 min incubation of 400 mm² copper strip in 5 ml. of protein solution. ○, Albumin in 0.9% NaCl; ●, albumin in water.

It was noticed that the portion of a copper strip immersed in albumin solution became dull due to precipitated protein on its surface, the portion of the strip extending into the air remained shiny, but a thin line of the air–albumin solution interface became black. Oxygen seems to play a role in the copper dissolution process.

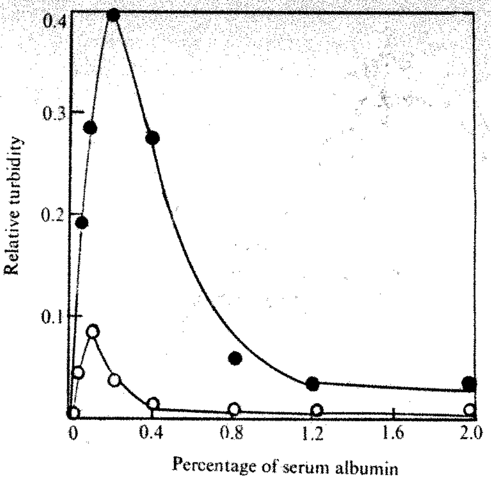

Fig. 2 Relative turbidity (absorbance at 500 nm for 1 cm path length) of copper-incubated albumin solutions. Conditions as in Fig. 1.

When oxidized and reduced glutathione (1×10^{-2} M) was incubated with copper strips, the former caused the formation of cupric ions whereas the latter showed only a slight reaction. These observations indicate that the disulphide bond is a critical group in the copper dissolution process by biological materials, presumably acting as an oxidizing agent in the oxidation of metallic copper to cupric ion. The reduction potential of glutathione is −0.35 V and the potential for the process $Cu \rightarrow Cu^{2+} + 2e$ is −0.337 V. The oxidation of copper by the disulphide bond is not more easily accomplished if the first step $Cu \rightarrow Cu^{+} + e$ (−0.521 V) is followed by the subsequent oxidation of cuprous to cupric ion by oxygen.

The precipitated protein illustrated in Fig. 2 is albumin with some S–S bonds broken. A saline-free 0.2% albumin solution without metallic copper but containing 7×10^{-5} M $CuSO_4$ did not precipitate after 90 min of incubation (compare with Figs. 1 and 2). The sharp maximum in turbidity arises from the precipitation of the modified albumin by cupric ions which can be reversed at high albumin concentration. If fresh albumin is added to a precipitated albumin solution which has been treated with metallic copper, the precipitate slowly disappears. Apparently, once cupric ions are formed, there is competition for these ions by both modified and normal albumin; the latter is well known to bind cupric ions although it is not precipitated at these low Cu^{2+} concentrations.

Other proteins which dissolve metallic copper include ovalbumin, insulin, alkaline phosphatase and carbonic anhydrase. The two enzymes lose their activity after incubation with metallic copper when a Cu^{2+} concentration of 7.5×10^{-5} M is reached. On the other hand, incubation without the metal but with 7.5×10^{-5} M $CuSO_4$ does not appreciably lower enzyme activity. This again indicates a modification of the proteins at the metal surface, rather than an action of cupric ions.

The finding that disulphide bonds oxidize metallic copper suggests a number of ways by which the copper intrauterine device might act. It may precipitate albumins and change the uterine wall in such a way as to prevent implantation; it may reduce stickiness of the uterine secretions and suppress implantation; it may lyse the mucoid materials which may then no longer provide a supporting medium for transport of spermatozoa; finally, crucial enzymes may be inactivated by the metal and cupric ions may kill sperm. Thus the reaction of biological substrates at a metallic copper surface results not only in the formation of cupric ions, but also in a drastic transformation of the physical and chemical characteristics of disulphide-containing biopolymers.

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Incidence of R^+ *Escherichia coli* in Coastal Bathing Waters of Britain

Escherichia coli able to transmit antibiotic resistance to pathogenic organisms has been found in British rivers, their principal source being insufficiently treated human sewage[1]. As sewage contamination is considered to be fairly widespread in coastal bathing waters in Britain[2], I have looked for these *E. coli* here.

Table 1 Concentration of Antibiotic-resistant Coliform Organisms in Seawater from Bathing Beaches

Beach	Viable coliform organisms per 20 ml.* resistant to antibiotic					Total
	C	T	S	N	A	
Penarth	5 (3–15)	50 (20–80)	50 (20–100)	4 (2–15)	500 (200–1,000)	4,000 (1,600–8,000)
Herne Bay	4 (1–16)	30 (20–70)	10 (2–40)	10 (0–2)	20 (3–40)	2,000 (250–8,000)
Sheerness	1 (1–5)	20 (10–30)	35 (20–40)	1 (0–1)	40 (30–60)	900 (400–1,600)
Ogmore	1 (0–4)	8 (3–30)	10 (2–40)	0 (0–1)	20 (5–70)	600 (200–800)
Clacton	1 (0–3)	10 (6–20)	9 (3–10)	2 (0–5)	5 (1–10)	300 (100–400)
Barry Island	1 (0–2)	7 (2–20)	10 (5–15)	0 (0–2)	45 (30–80)	400 (300–600)
Ramsgate	0 (0–1)	4 (1–8)	2 (1–4)	0 (0–3)	3 (1–15)	100 (50–250)
Whitstable	0 (0–4)	2 (1–30)	2 (1–20)	0 (0–4)	4 (0–20)	250 (50–2,000)
Canvey Island	1 (0–4)	3 (1–7)	1 (0–2)	0 (0–1)	30 (8–30)	200 (50–400)
Broadstairs	0 (0–3)	3 (1–8)	3 (0–6)	0 (0–1)	5 (3–10)	150 (50–800)
Lowestoft	0 (0–1)	2 (0–4)	2 (0–3)	0 (0–0)	1 (0–5)	100 (20–400)
Yarmouth	0 (0–1)	2 (0–3)	2 (0–3)	0 (0–0)	3 (1–8)	200 (100–400)
Eastbourne	0 (0–0)	0 (0–2)	0 (0–8)	0 (0–2)	0 (0–3)	10 (0–30)
Margate	0 (0–0)	0 (0–3)	0 (0–0)	0 (0–0)	0 (0–20)	6 (0–40)
Brighton	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	1 (0–3)

C, Chloramphenicol; T, tetracyclines; S, streptomycin; N, neomycin; A, ampicillin.

* Median count followed by, in parentheses, the range of counts for ten samples collected on the same occasion from different sites on the beach.

Samples of seawater (250 ml.) were collected in sterile glass containers, usually from both ends of each beach and at eight approximately equidistant intermediate sites. They were collected a few metres from the shore at high water because this is the most common time for bathing, although while the survey was performed (spring 1971) the beaches were rarely used for this purpose. The beaches were randomly chosen for sampling in that no information had been sought on the disposal of sewage in their vicinity.

The numbers of viable antibiotic-resistant and sensitive coliform organisms in the samples of seawater were estimated by the method previously used to examine river water[1], except that the Petri plates of MacConkey's agar containing different antibiotics were each inoculated with the centrifuged deposit of 20 ml. of each sample instead of 1 ml. of each sample. The methods used in the river water studies were also used to identify coliform organisms as *Escherichia coli* of faecal origin, to determine their antibiotic resistance pattern and to discover if their resistance was transmissible.

The results of examining ten samples of seawater collected on the same occasion from each of fifteen bathing beaches are summarized in Table 1. There was great variation in the concentration of antibiotic-resistant coliform organisms in samples from the different beaches. For example, relatively large numbers were isolated from all ten samples collected at Penarth, whereas none were isolated from the ten collected at Brighton. From some beaches, such as Whitstable, only one or two samples contained high concentrations of antibiotic-resistant coliform organisms.

The results of examining seawater from the same ten sites on Southend beach, some 7 km long, on seven occasions, 14–21 days apart, differed greatly (Table 2). For example, very few coliform organisms, resistant or sensitive, were isolated from any of the ten samples collected on the first occasion whereas relatively high concentrations were found in those collected on the fifth occasion, a day when the sea was unusually turbulent and there was a strong onshore wind. On four occasions, considerably higher numbers of coliform organisms were isolated from water from one or two sites than from the water from the other sites, but the particular sites involved were not the same on each occasion.

In general, the ratio of the concentrations of the different kinds of antibiotic-resistant coliform organisms to each other and to the antibiotic-sensitive organisms in the seawater resembled that in human sewage[1]. Three specimens, however, contained unusually high proportions of coliform organisms possessing the same antibiotic-resistance pattern; one of these contained 2,000 coliform organisms in 20 ml., more than 75% of which were resistant to neomycin, streptomycin and sulphonamides.

The Eijkman test was done on a representative collection of strains of coliform organisms isolated from all bathing waters examined. On the basis of this test, seventy-eight of eighty-three strains isolated because they were chloramphenicol-resistant were classified as faecal type *E. coli*. The corresponding figures for tetracycline-resistant strains were 107 of 111, for streptomycin-resistant strains were sixty-eight of ninety-four, for neomycin-resistant strains were forty-two of forty-five, for ampicillin-resistant strains were fifty-two of 100 and for fully antibiotic-sensitive strains were seventy-four of 138.

Table 2 Concentration of Antibiotic-resistant Coliform Organisms in Seawater on Different Occasions from Southend Beach

Occasion	Viable coliform organisms per 20 ml.* resistant to antibiotic					Total
	C	T	S	N	A	
1	0	1	1	0	5	30
	(0–0)	(0–4)	(0–4)	(0–1)	(0–10)	(5–60)
2	0	0	0	0	2	20
	(0–0)	(0–30)	(0–4)	(0–0)	(0–40)	(10–100)
3	1	3	4	0	70	200
	(0–3)	(0–30)	(0–20)	(0–6)	(0–200)	(40–1,000)
4	0	2	1	1	10	50
	(0–5)	(0–60)	(0–50)	(0–3)	(0–40)	(50–300)
5	3	25	25	3	100	1,200
	(0–15)	(10–150)	(3–2,000)	(1–2,000)	(20–2,000)	(400–8,000)
6	1	15	10	0	30	600
	(0–6)	(1–40)	(0–20)	(0–2)	(0–100)	(400–2,000)
7	0	4	1	0	7	150
	(0–3)	(0–200)	(0–20)	(0–0)	(0–60)	(40–4,000)

*For other details see Table 1.

Most of the antibiotic-resistant coliforms were resistant to more than one antibiotic. Some were resistant to five or six; this was particularly so in the case of those isolated because they were resistant to chloramphenicol or neomycin.

Forty-six of fifty-four strains of coliform organisms isolated because they were chloramphenicol-resistant transmitted their resistance to *E. coli* K12F⁻ in mixed culture. The corresponding figures for tetracycline-resistant strains were fifty-six of seventy-seven, for streptomycin-resistant strains were thirty-six of seventy-seven, for neomycin-resistant strains were thirty-three of thirty-six and for ampicillin-resistant strains were twenty-five of seventy-six. Of twenty multiply resistant strains isolated from different samples of seawater on account of their chloramphenicol resistance, eighteen transmitted their resistance to *Salmonella typhi*.

Broth cultures of five strains of faecal *E. coli*, possessing different antibiotic resistance patterns and isolated initially from bathing waters, were added to different samples of seawater in amounts sufficient to give a final concentration of 10,000 viable organisms per ml. The samples were then kept at room temperature. After 1 day, the concentration of the resistant organisms in the samples had decreased by 0–60%. After 2, 3 and 4 days, the corresponding percentages were 25–80, 50–100 and 97–100 respectively. No resistant organisms were found in any of them after 5 days.

Some coliform organisms found in seawater and identified by biochemical tests as faecal type *E. coli* might have originated in marine life or wild birds. The presence of R^+ forms of such organisms in seawater provides stronger evidence of contamination with human sewage, particularly when the composition of the coliform population resembles that in human sewage, as mentioned before. On this basis, some of the bathing waters examined seemed to be relatively heavily contaminated throughout their length, or in localized regions only, and others did not. The great variations between the results of the examinations of Southend seawater collected on different occasions clearly indicated, however, that freedom from contamination cannot be determined from the result of one set of examinations only. The heaviest degree of contamination at Southend was found on the occasion when the sea was most turbulent due to a strong on-shore wind, supporting the view that such conditions may favour beach pollution[2]. A sample of seawater in which *E. coli* of one particular antibiotic resistance pattern comprised practically the whole of its coliform content can only be explained by assuming that the sample contained a particle of faeces from an individual who had recently been treated with an antibiotic.

It is a reasonable assumption that bathing waters contaminated to the extent of some in our survey may play a part in the dissemination of R^+ *E. coli* in the human community. They may also play a part in the dissemination of pathogenic organisms. The lack of incriminating evidence cannot be accepted as proof that they are of little importance in this respect. As far as the R^+ *E. coli* are concerned, the laboratory studies showed that they did not live for long in seawater, indicating that the sea is a temporary reservoir only of these organisms. Consequently, the present undesirable situation could be corrected immediately if proper disposal of sewage from seaside towns were practised.

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Illusions in Perspective

DR HUMPHREY speculates on the thought processes of the Sung school and Italian primitive painters[1]. I, too, was puzzled by distortions in the tenth century "Midsummer Rest under a Locust Tree" and in Ugolino's "Resurrection".

If you apply a ruler to the graphic illustrations in Dr Humphrey's paper, it seems that the back edge of the philosopher's couch in Fig. 5 is in fact some 2 mm longer than the front; the corresponding inside dimensions of the lid of Christ's sarcophagus in the photograph in Fig. 6 differ by about 1.5 mm. Whatever the artists thought they were up to, they should not be accused of confusing their trapezoids with what Dr Humphrey perceives as a "perfect parallelogram". Not that I wish to question his explanation of the artists' distortions in terms of "mediaeval practice to prefer a formal rule to the mundane evidence of the senses".

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Contrast Illusions in Perspective

THERE seems to be some confusion in Humphrey's account of "Contrast Illusions in Perspective"[1]. This may be due to over-compression, especially of a crucial paragraph (page 92, para. 3), which contains: "The nature of the optical projection to the eye is such that more distant objects on the whole give rise to smaller retinal images than near ones, and distance is therefore a guide to retinal size. The expected size of the further of two objects is less than that of the nearer, and hence if we see two lines which appear to be different distances but have the same actual length, we judge the further to be longer than the nearer". There are some curious features in this which though perhaps obvious should be spelled out, to avoid an already confused situation being worse confounded. (1) It is clearly not retinal image size which Humphrey supposes is "guided" by distance. Image size is given directly, by the geometry of object size and distance and the optical characteristics of the eye. The intended meaning must surely be along the lines of "perceived size"; but this is a very different matter from retinal image size—hence, indeed, the problem. (2) It is not the expected size of objects, lying at various distances, which is the issue but the image size corresponding to various object distances. (This is given directly by object size and distance, as stated.) (3) Perceived size (assuming this is what is meant, in place of "retinal size") cannot be given by distance *per se*. It would have to be given (or "guided") by available information of distance. This could be real-time sensory data; or it could be stored information, as of the shapes of familiar objects, such as tables.

It is a matter for experiment to discover the kinds of sensory data used for giving perceived size and distance. We know that perspective convergence of parallel lines and texture gradients are important; especially so for vision with a single fixed eye, as in viewing pictures. We know less about which object shapes are assumed for inferring size or distance from familiar objects; but we know this does occur, for example, from experiments with depth-ambiguous wire figures which change apparent shape as perception changes, though the retinal image (real-time sensory data) remains constant[2].

(4) Again we cannot suppose that signalled distance is a guide to retinal image size. Image size is given directly from the geometry of the situation (as stated in (1) above) and so cannot be "guided" by distance *per se* or by available (real-time or stored) information of distance. If, however, Humphrey does mean by "retinal size" something like "perceived size" or "apparent size", then he is saying that signalled or assumed distance affects perceived size. This is certainly so: it follows from the classical Emmert's law demonstration, from depth-ambiguous wire figures which change their shape with depth reversals[2] and many other demonstrations. But it is perceived size and not retinal size which changes as a function of signalled or apparent distance. To confuse the two is to wreak havoc with any discussion of these problems.

(5) Although for the normal world of objects sensory information and assumed distance affect perceived size, the case of line pictures is complicated by the fact that they are seen both as flat patterns of lines on a flat background which they physically are, and as depicted objects, in a different space, which they represent. The distortions evidently follow the depicted distances, rather than the physical distances which indeed are absent for a physically flat picture. Several implications follow. An account of the phenomena simply in terms of retinal patterns and directly associated physiological activity can hardly be adequate, for it is the significance of the patterns in terms of familiar objects, especially their usual shapes, which are determining apparent size. (This takes us to concepts like "software" computer concepts. Accounts in purely physiological terms seem inadequate, for they cannot handle significance or probabilities of object characteristics. Hence the need for "cognitive" concepts in perceptual theory. Cognitive processes will, however, be mediated by physiological processes—as computer hardware mediates the "software" mathematical and logical processes of a computer. Given the physiological/cognitive distinction, errors of size might be attributed to errors in physiological processes, mediating cognitive "programmes", or inappropriateness of the programmes themselves.

By invoking "expectancy" Humphrey is calling on a cognitive concept. I would agree that this is appropriate for the rectilinear projection distortions, though not for the "waterfall" after-effect of motion, in which object recognition is not involved. (The induced motion of the "waterfall effect" does not, as an after-effect of retinal image motion, depend on object recognition, either for inducing it or observing it.)

There is something odd, at least at first sight, about explaining something unexpected (the queer shapes of tables drawn in rectilinear projection) in terms of expectation. How can expectation give unexpectedness? I think it can, but the argument requires another and vital step. We may plausibly suppose that the usual perceptual scaling constants are applied to rectilinear projections of objects, much as though the depicted objects were seen with the normal perspective of retinal images when viewing the objects directly. Image size normally shrinks with increased object distance (giving retinal perspective), and this is normally compensated (giving size constancy), so we should expect depicted distance to be associated with expansion, in these zero-perspective pictures—if normally appropriate size scaling is evoked by the "recognition" of the picture as depicting an object, such as a table. Humphrey correctly points out that the distortions increase as the pictures are drawn more lifelike, apart from the absence of perspective. The more strongly it is recognized as a table, the greater the distortion. We may, I believe, describe the distortions by saying that the usual perceptual size corrections for compensating image shrinking with object distance are operating, according to the depicted objects, but that this is inappropriate for these pictures because there is no perspective to compensate[3]. Features depicted as more distant are perceptually expanded. They are expanded by the size scaling, itself established by many experiments, which normally compensates retinal perspective shrinking, to give size constancy in the three dimensional world of normal objects. In rectilinear projections there is no perspective shrinking with depicted distance: so the normally appropriate corrective scaling is inappropriate—and so generates the observed distortions. Is there any reason not to believe in this account of the matter?

Finally, to say that "expectancy" and "contrast" are concepts applicable to illusions ranging from colour changes after wearing red glasses, the "waterfall-effect" of induced movement, the "size-weight" illusion, after-effects of size, as well as the rectilinear projection illusions and presumably also perspective illusions, is either to have a deep insight into the mechanisms of perception or to give such a low resolution description that important differences between them are blurred.

A vital distinction which should not be lost is between (*a*) neural systems becoming modified, or adapted, by maintained or unusual stimulation ("physiological adaptation"), or by prolonged or unusual sensed object-characteristics ("cognitive adaptation") and (*b*) normally functioning physiological or cognitive processes, being applied inappropriately in the given situation. Inappropriateness can generate errors and distortions in unusual situations though the system is functioning normally; but to recognize that this is the case we must understand the significance of the physiological and cognitive processes, and discover why they are inappropriately applied, and in what ways they are inappropriate, in the illusion situation. This involves looking at each illusion situation very carefully: facile generalizations prevent our seeing the significance of the phenomena in terms of normal but misapplied, or abnormal, functioning of the perceptual system. Perhaps a theoretical classification is needed here; the following seems useful: (*A*) physiological illusions, generated by physiological (1) adaptation, (2) inadequacy, (3) inappropriateness; (*B*) cognitive illusions, generated by cognitive: (1) adaptation, (2) inadequacy, (3) inappropriateness. Although there is much room for debate and further knowledge, all illusions can, I submit, be classified with these headings without doing damage to distinctions we need to bear in mind to understand perceptual effects and use the phenomena as tools for understanding perception.

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Model for a Two-adversary Arms Race

A MATHEMATICAL model for a two-adversary arms race which comprises three features, (i) response to adversary's stockpile, (ii) response to his growth rate and (iii) finite resource limitation, can be described by the pair of equations

$$u_1' = (K_1u_2 + L_1u_2')\,(a - u_1) \qquad (1)$$

$$u_2' = (K_2u_1 + L_2u_1')\,(b - u_2) \qquad (2)$$

where u_1 and u_2 are the arms stockpile for the two sides; the primed functions, their time derivatives; and a and b, the finite limits to the resources of each. The factors $(a-u_1)$ and $(b-u_2)$ have been used before[1] to describe logistic growth laws, but make the above two equations non-linear.

In this model the responsive coefficients are non-negative constants. If both u_1 and u_1' are positive, so must u_2'. Should one's stockpile be kept stationary ($u_1'=0$), the foe's will still grow ($u_2'>0$) by the second equation. A slight decrease in one's stockpile (u_1' negative but small) will not prevent the foe's growth (u_2' positive by equation (2)) which, in turn, induces a renewed growth in one's stockpile (by equation (1)). Slight rates of disarmament by either side, or both, is not a stable condition. There is an ineluctable return to competitive growth.

There is a critical rate for one's own arms reduction rate, when $K_2u_1 + L_2u_1' = 0$, which induces the foe to keep his stockpile level constant. From this critical condition one's stockpile has an exponential decay with relaxation time L_2/K_2. Disarming slower than this leads to the above mentioned instability; more rapidly, to the foe's disarming. However, one's disarmament rate must be even more drastic than this to attain stable bilateral disarmament. For, if the adversary's induced disarmament rate is slight, one's own rearmament will be induced. That condition is

$$u_1' < -K_2u_1/L_2 - K_1u_2/L_1L_2$$

From this, the greater is each stockpile the greater the response to these, and the less the response to the rate of reduction, the more drastic must one's disarmament rate be to induce the foe to disarm rapidly enough to, in turn, assure oneself. By interchanging subscripts the foe's condition is obtained. The solution of these two simultaneous inequalities has two exponential decay terms. For simplicity, if $K_1 = K_2 = K$ and $L_1 = L_2 = L$, these are $\exp -K(1 \pm 1/L)t/L$. The term with the upper sign is the faster and proper decay.

If bilateral disarmament does not obtain, the ensuing arms race can be examined. In the light of the high priority given to a nation's military capability it is reasonable and certainly convenient to neglect the factors $(a-u_1)$ and $(b-u_2)$ in the first equations. These can then be restated as two second order equations

$$(1 - L_1L_2)u_1'' - (K_1L_2 + K_2L_1)u_1' - K_1K_2u_1 = 0$$

and, *mutatis mutandis*, the same for u_2. Note that the constant coefficients are identical for u_1 and u_2. If the first coefficient were negative, it would not be possible to have u_1, u_1', and u_1'' all positive or all negative. Since there is no obvious self-correction of this sort in an arms race, L_1L_2 cannot exceed unity.

For the special case $L_1 = L_2 = 0$, there is an exponential growth with argument $(K_1K_2)^{\frac{1}{2}}t$, and the familiar Lanchester N-square law[2]

$$u_1^2/K_1 = u_2^2/K_2 + \text{constant}$$

When $K_1 = K_2 = 0$, it follows that $L_1L_2 = 1$. The two-terms solution of the second order equations is particularly simple if corresponding responsive coefficients are identical, so the subscripts may be omitted.

$$u_1(t) = \tfrac{1}{2}(u_1(0) \pm u_2(0)) \exp \pm Kt/(1 \mp L)$$

Similarly, for $u_2(t)$. The adversary with the initially smaller stockpile will grow faster until both sides have identical increasing capabilities (provided the finite-resource constraint is not imposed). The growth term increases explosively as L approaches unity. In this model greater response to rate of growth corresponds to more rapid escalation.

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[1] Blumberg, A., *J. Theoret. Biol.*, **21**, 42 (1968).
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BOOK REVIEWS

Science and Synthesis

Interpretations of Life and Mind. Edited by Majorie Grene. Pp. xvi+152. (Routledge and Kegan Paul: London, October 1971.) £2.25.

CAN anything change the headlong course of history towards greater disasters? The doctrines and religions of the past have failed to promote peace and goodwill. For some the only hope lies in the emergence of a scientific and philosophical synthesis providing not only a better image of man but a compelling vision of what mankind must achieve in this century. This major humanist aim lies behind the title of this volume. In 1965 UNESCO summoned an international colloquium of some forty scholars in memory of two world figures who died in April 1955 and provide symbols of the unifying imagination seeking to construct respectively a scientific/mathematical and a philosophical/ethical cosmology. This report, a late translation from the French edition of 1967, contributes little to the major aim, but contains much of interest on physics.

The main themes covered are Einstein and the scientific synthesis, debates on science and synthesis, and Teilhard de Chardin. The papers on the first two, with one important exception, deal principally with cosmological myths and theories, advanced physical theory, and Einstein's thought. Two call for mention: first, J. R. Oppenheimer's perceptive note on Einstein and the three traditional elements which deeply influenced him—the statistical mechanical interpretation of thermodynamics, the concept of the field, and the principle of sufficient reason—and second, a most interesting twenty-five page study by G. Holton, using unpublished letters, of the relation of Einstein's changing philosophy of physics to Mach's positivism.

Most of the special topics discussed are old, but it is useful to have the fairly recent views of W. Heisenberg, L. de Broglie, and others on the unified field theory, from plurality to unity, determinism and indeterminism, and the organization of scientific research.

The final section on de Chardin expresses appreciation of his personality, his work on palaeontology, and his philosophical and religious doctrine. Scientists should be tolerant of speculative visions, for history shows that they can prove fertile and we are in need of unifying principles. However, in the preface to his *Phenomenon of Man*, de Chardin, surely unwisely, said that this book "must be read purely and simply as a scientific treatise". Why, then, do his supporters here fail to make a critical analysis of his ideas and to set them in their historical context since several influential thinkers—Bergson, Whitehead, Smuts, and Sir Julian Huxley *inter alia*—have expressed similar views?

The exception referred to is a humanist manifesto by Huxley, who alone examines the perils ahead and how science and synthesis might help. Huxley is strong on diagnosis, but weak on therapy, like nearly all as yet. He identifies, correctly I suggest, four current insanities: military reliance on the H-bomb, economic on the profit motive, political on competitive power units, and biological on unrestricted human reproduction. When Huxley concluded, did those in agreement stand up to be counted, as a tiny nucleus of a future world consensus of the sane? Will UNESCO respond to his plea and continue the debate on the "new organized system of thought and belief (which) is the greatest task of this generation"?

A weakness of this volume is that biological synthesis is not discussed and molecular biology barely mentioned. Was not the Crick/Watson discovery of 1953 an authentic synthesis, perhaps as fertile in its own way as Einstein's metrical tensor law of 1916? This and other limitations are inevitable. So vast a theme could not be covered in this slim volume, for which we must be grateful; parts of it are excellent.

LANCELOT LAW WHYTE

Evolution of Physics

Bergson and the Evolution of Physics. Edited and translated by P. A. Y. Gunter. Pp. xi+348. (University of Tennessee: Knoxville, 1969.) $10.50.

IN the introduction to this collection of essays Professor Gunter presents first a short history of Bergson's life. In spite of the immense success which followed the publication of *L'Evolution Créatrice* in 1907 (Bergson was then forty-eight years old), dark elements were not lacking in his life. The great vogue lasted only a few years, till the First World War. Then his writings were attacked with increasing violence. His influence declined and at the moment of his death in 1941, after years of illness, his way of thinking was already associated in the mind of many people with an aura of mysticism and anti-intellectualism. Even today it is often fashionable to present a few derogatory remarks about his philosophy (ref. 1 provides a recent example). Therefore the book edited by Gunter is most timely. It contains four parts: quantum physics (contributions by Louis de Broglie, Satosi Watanabé, Olivier Costa de Beauregard, Robert Blanché), relativity (Henri Bergson, Albert Einstein and Henri Piéron, André Metz and Henri Bergson, Günther Plug, J. F. Busch, W. Berteval, Olivier Costa de Beauregard), Bergson and Zeno's paradoxes (Vere C. Chappell, David A. Sipfle) and a concluding summary by Malič Čapek. Most of these articles appeared originally in French or German and have been translated for this book. Except in the section on relativity there are no original texts by Bergson.

"We interpret the past through the present." This saying is well illustrated by Louis de Broglie's article who, in his words, has "been struck by the analogy between certain new concepts of contemporary physics and certain brilliant intuitions of the philosophy of duration". The section on relativity, while it is the longest, is unfortunately the least interesting. As is well known, Bergson's specific method in metaphysics is based on what he called "intuition" and according to his words: "penser intuitivement est penser en durée"[2]. He felt therefore that relativity with its spatialization of time was a threat to his views. Today it may be safely stated that time is no more and no less spatialized in relativistic physics than it is in pre-relativistic physics. It is as meaningful to speak of irreversibility and increase of entropy as it was before. Bergson's struggle with the Lorentz transformation in "Durée et Simultanéité" is as pathetic as it completely misses the point. In his article "The Principle of Relativity and the Spatialization of Time" de Beauregard comes closer to the issue when he notes that "Einstein's great discovery and Bergson's just claims may be less incompatible than they appear at first glance". Indeed in a recent paper Balescu and Brenig[3], using the recent developments in statistical mechanics, were able to prove that all relaxation times are invariants in respect to the Lorentz transformations.

Analysing the durée, Bergson reached the conclusion that time had to have attributes quite foreign to classical dynamics: "Plus profondément nous pénétrons l'analyse de la nature du temps, mieux nous comprenons que durée signifie invention, création de formes, élaboration continue de ce qui est absolument neuf"[4]. It is indeed quite remarkable how close these views are from those reached in thermodynamics of irreversible processes (see especially refs. 5 and 6).

At the third meeting of the Institut de la Vie, devoted to theoretical physics and biology (Versailles, June 1971), Szent-Györgyi made the following chairman's remarks (preprint): "... We all studied one or another part of living systems. The smaller the unit, the more pure physics and chemistry, but also the less 'alive' it is. . . ."

It is fascinating to compare this text with the following one by Bergson (*L'Evolution Créatrice*, page 31, oeuvres page 521): ". . . Ainsi la 'vitalité' est tangente en n'importe quel point aux forces physiques et chimiques ; mais ces points ne sont, en somme, que les vues d'un esprit qui imagine des arrêts à tels ou tels moments du mouvement générateur de la courbe. En réalité, la vie n'est pas plus faite d'éléments physico-chimiques qu'une courbe n'est composée de lignes droites."

It seems to me a weakness of this otherwise very valuable book that these important aspects have been neglected.

I. Prigogine

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[2] Bergson, H., *La Pensée et le Mouvant*, 30; (Ouevres, ed. du Centenaire, Presses Universitaires de France, Paris, 1963).

[3] Balescu, R., and Brenig, L., *Physica*, **54**, 504 (1971).

[4] Bergson, H., *L'Evolution Créatrice*, 11 (Oeuvres, 503).

[5] Glansdorff, P., and Prigogine, I., *Structure, Stability and Fluctuations* (Wiley Interscience, New York, 1971); (French edition by Masson, Paris, 1971).

[6] Eigen, M., "Self-organization of Matter and the Evolution of Biological Macromolecules, Ch. VIII, sect. 5, *Naturwissenschaften* (in the press).

Russian Crystals

Symmetry of Crystals. By E. S. Fedorov. Translated from the Russian by David and Katherine Harker. Pp. x+315. (American Crystallographic Association: New York, 1971.) $25.00.

One of the great scientific activities of the nineteenth century was classification. In many fields the systems then developed have long since fallen into disuse, but the most modern work in X-ray diffraction still makes use of the idea of the crystallographic space groups which were discovered, apparently independently, by Fedorov somewhere between 1885 and 1890, by Schoenflies in 1891, and by Barlow in 1894. Unfortunately, because Fedorov's work was published in Russian, it did not become widely recognized in the West until after the other two publications. The three authors approach the subject from quite different points of view and Fedorov's is based on a geometrical system of his own development which involves consideration of the ways in which space may be filled by polyhedra of different shapes.

In 1949 the USSR Academy of Sciences commissioned the publication of a collection of Fedorov's contributions divided into five monographs. The first three set up the basic analytical geometry required and consider the necessary ideas of symmetry. Monograph four is Fedorov's own comparison with the results of Schoenflies, and in monograph five Fedorov develops the ideas of space-filling polyhedra.

The present work is a translation of the 1949 Russian text and is obviously a labour of love. The project was undertaken by the National Science Foundation and the American Crystallographic Association, and it goes without saying that a work of this magnitude and complexity could not possibly have been translated adequately except by someone as familiar with the scientific material as with the Russian language. Dr and Mrs Harker clearly satisfy these conditions and their magnificent version is a real contribution to the historical documentation of crystallography.

It is, however, very much more than a mere historical document. The ideas and developments followed by Fedorov are most stimulating though the somewhat ponderous prose—which undoubtedly is an accurate reflexion of the nineteenth century atmosphere—may be a little daunting to some readers.

It should certainly find a place in the libraries of all crystallographic laboratories, and all concerned in its production are to be congratulated on making such a fascinating document readily available to modern crystallographers.

C. A. Taylor

Narcotic Pharmacology

Narcotic Drugs: Biochemical Pharmacology. By Doris H. Clouet. Pp. xxii+506. (Plenum: New York and London, 1971.) $31.36.

Although the opium alkaloids have been used for medicinal purposes in one form or other for more than two thousand years, we still do not understand how these drugs and their modern synthetic and semi-synthetic congeners exert their analgesic action and why they produce such severe physical dependence even after a relatively short period of use. In recent years, the interest in these drugs has risen steeply, chiefly because of their widespread non-medicinal use by persons who have become dependent on them. A great deal of effort has been spent by research workers in universities, research institutes and pharmaceutical firms to produce new compounds which retain their analgesic power but are not liable to be abused as drugs of addiction.

The volume edited by Dr Clouet brings together some of the work published in recent years. The subtitle of *Biochemical Pharmacology* is rather a misnomer because the twenty-six chapters range over a much wider area of the pharmacology of the narcotic analgesic drugs than could be defined as biochemical. The contents cover the chemistry of narcotic analgesic drugs, their metabolic disposal, their effects on the metabolism of energy, phospholipids, proteins and nucleic acids, their effects on biogenic amines, acetylcholine, corticosteroids and other hormones. The sites and modes of action of the narcotic analgesic drugs are examined in single cells, the central and peripheral nervous system and the kidneys. There is a discussion of the possible causes of tolerance and, finally, a consideration of two important therapeutic programmes, namely the use of antagonists as a protective measure and the methadone maintenance programme.

It is unfortunate that most of the research work reported in this volume was published before naloxone, the first pure antagonist of morphine, had become available. In many of the papers quoted, the partial agonists, nalorphine and levallorphan, served as "antagonists"; because of their dual action as agonist and antagonist, the interpretation of the experiments in which they were used was often equivocal. Until the advent of naloxone, it was not easy to distinguish between specific and non-specific effects of morphine-like drugs. This dilemma was particularly difficult to overcome in experiments on certain isolated tissues in which only very high concentrations of these drugs had an effect. We know now that many of these effects are non-specific; apart from not being antagonized by naloxone they also do not show such stereospecificity as is found for their analgesic effects. It is for these reasons that some of the observations and conclusions presented in the volume cannot be accepted as valid.

The editing of books written by a number of authors is a difficult task of which Dr Clouet has absolved herself well. Nevertheless, a few unfortunate phrases have not been expunged, as for example "illicit narcotic seizures also have been analysed by microcrystal tests".

My criticisms should, however, not detract from the importance of this book which will be of great value to the active research worker who feels with L. Shuster that "theoretical castles are easy to build in the realm of narcotic addiction" and with H. L. Borison that "so long as we lack more effective means of studying the communication mechanisms of the brain, we shall have to face the dilemma as to how the neurochemical approach to addiction can yield meaningful answers if they do not rest upon sound neurophysiological footing".

H. W. Kosterlitz

CORRESPONDENCE

Space Research

SIR,—May I as one of the founder members of the European Space Research Institute (ESRIN) at Frascati, Rome, thank you for bringing to the attention of your readers the dangers facing that institute. A proposal to close the institute was accepted as part of the basic plan for the future programme by the council of ESRO of July 14 subject to definite adoption in November. This action has been widely considered as a setback to the cause of European scientific collaboration.

This situation is of importance at this moment when there is a probability of growing collaboration in Europe and I would like to consider it in the light of Professor Sir Brian Flowers's recent article in *Nature* on "Science and the Common Market". In this article he proposed five criteria for successful collaboration in science. For brevity I shall paraphrase these five criteria as follows: (*a*) the need to establish a scientifically viable institute; (*b*) that the institute should have a part to play in European science; (*c*) that it should be supported wholeheartedly by the collaborating nations.

Let me now consider to what extent ESRIN has satisfied these criteria. Those of us who worked together to build ESRIN believed that there was a need for a European institute devoted to space physics and that ESRIN could fulfil that need despite the severe restriction imposed on it that any direct participation in satellite or rocket experiments was precluded. The contributions made to the field of space physics are exemplified by the following: theoretical studies of the magnetosphere, laboratory simulation of magnetospheric and ionospheric phenomena, collaboration in European experiments on gravitational waves and in design of a cosmological satellite experiment; studies of the solar corona with reference to heating mechanisms and spectroscopic observations; development of a high resolution laser scattering technique for atmospheric studies; design of a new high aperture, high resolution electrostatic spectrograph for particle analysis in the ionosphere and of novel multichannel recording systems (patented); and so on.

I believe that the breadth and depth of these contributions indicate that in less than three years of full operation ESRIN has achieved a high degree of viability. Perhaps this is best demonstrated by the fact that protests against the proposed closure have been made by many scientists including Professor Alfvén, Professor Biermann, Professor Lehnert, Professor Parker and Professor Van Bueren.

The programme, and the budgetry means to carry it out, have also been approved by the council of ESRO each year up to and including 1971. Why then has it been considered that this viable and internationally recognized institute should be closed; that in the future ESRO cannot support its budget of $2 million out of a scientific research budget of $27 million and a total budget of $70–80 million?

The new plans for ESRO indicate a changing programme for the organization as a whole and it is reasonable to expect the programmes of each part of ESRO to reflect these changes. Not to allow this to take place at ESRIN, but to abandon the capabilities to carry out research on the European scale built up at considerable expense to the taxpayer, would appear to be an act of irresponsibility.

It seems to me therefore that the explanation for the action lies more deeply than this change in programme. I believe it arises from the problem of "in house" research which has dogged not only ESRIN, but ESRO, from the start. The policies being evolved for execution of the new programme call for further reductions of "in house" research; the closure of ESRIN would be but one of the reductions.

Surely, as stated by Sir Brian Flowers in his article, the lesson of the success of CERN is that it has satisfied his five criteria and that the success is due in part to the complete collaboration and support of a central research laboratory and research group, that is, of "in house" research.

In choosing not to follow the example of CERN, and, in doing so, to close one of its viable and internationally recognized research centres, ESRO will find it more difficult to retain its own viability as a research organization.

Yours faithfully,

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Obituary

Professor Asher Korner

ON September 22, Professor Asher Korner died after some months of illness at the age of forty-four. Since 1967 he was Professor of Biochemistry in the School of Biological Sciences at Sussex University. He started his research career as a graduate student in the Department of Biochemistry at Cambridge working with Professor F. G. Young on the influence of androgens on growth. During the course of this work he became in the early fifties one of the pioneers developing cell-free systems capable of incorporation of amino-acids into protein. By the mid-fifties he had shown that microsomes from hypophysectomized rats were deficient in their protein synthesizing capacity and that this deficiency could be rapidly reversed by an injection of growth hormone to the whole animal. He went on to develop the first cell-free system from rat liver consisting of ribosomes freed from membranes and cell sap, which was capable of protein synthesis, and with this system he showed that the lesion in hypophysectomized animals lay in the ribosome fraction.

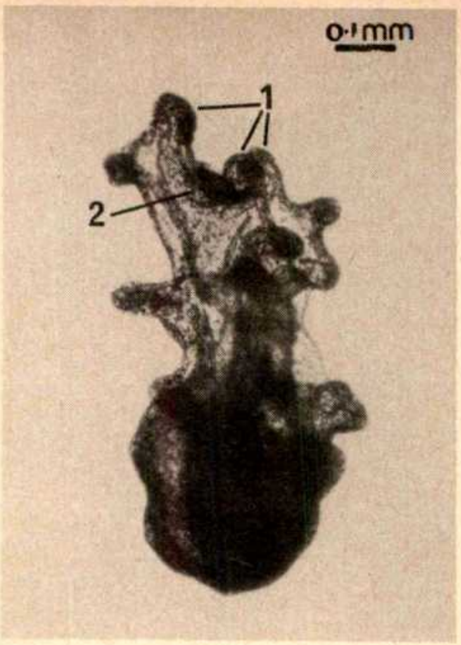
In the early sixties with the development of the messenger RNA concept it seemed that the effects of growth hormone on protein synthesis and growth could be explained in terms of its control of messenger RNA synthesis. Careful detailed research showed repeated inconsistencies in this model. By the mid-sixties his working hypothesis for the control by growth hormone was that this control was affected at the point of initiation of new rounds of protein synthesis on messenger RNA molecules. He thus became one of the first exponents of the new popular concept of controls on protein synthesis at the cytoplasmic level. Further he believed that the effects of growth hormone on RNA synthesis were secondary to its effects on protein synthesis. These concepts were the basis for his most recent research on the mechanism of initiation of protein synthesis and the interrelationship between protein and RNA synthesis. In summary he has made a major contribution to the development of the ideas and concepts which are now known as molecular biology and their application to the field of hormonal control of protein and nucleic acid metabolism, particularly the control of protein synthesis brought about by growth hormone.

Apart from his personal research achievements Asher Korner was an able and inspiring teacher both of graduates and undergraduates. His style of research, knowledge and enthusiasm helped the many graduates, students and associates who worked with him. His leadership created an environment in which learning and research flourished. In 1967 he left Cambridge to become the first Professor of Biochemistry at Sussex University where he quickly established a flourishing group of young and able biochemists.

Above all Asher Korner was an unusually kind and generous person. His loss is a blow to science in general but these personal qualities make his death particularly tragic to those who knew him well.

Erratum

In the article "Larval Development and Metamorphosis of *Acanthaster planci* (Asteroidea)" by J. A. Henderson and J. S. Lucas (*Nature*, **232**, 656; 1971), Fig. 2 should have been as follows:



Reports and Publications

not included in the Monthly Books Supplement

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Rothschild's Cat for all Pigeons

THE publication of the Rothschild and Dainton Reports (see page 169) marks the beginning of yet another period of heart-searching about the organization of British science. The chances are that the process will on this occasion be a good deal less gentlemanly than in the past —even the fierce arguments which there were about the Trend Report, which appeared in 1963, will by comparison appear like academic squabbles. For on this occasion, at least if Lord Rothschild has his way, blood will be spilled.

Both documents are organizational in the sense that they describe new frameworks within which the relationships between existing units may be re-adjusted. The Dainton proposal is, however, strictly passive—the Council for Scientific Policy which at present advises the government on policy in civil science would be replaced by a stronger body, called provisionally a board, with executive responsibility (to the Department of Education and Science) for apportioning funds between the research councils and, in the course of time, for creating new research councils or for abolishing those which have outlived their usefulness. In such a setting, so the Dainton argument goes, it would be possible for the research councils to evolve a more natural and dynamic balance between themselves. Lord Rothschild's proposals for the framework for the research councils are superficially similar but qualitatively quite different, for they introduce the concept, unfamiliar in Britain, that at least a part of what the research councils have to spend on civil science should be in the gift of the government departments most likely to benefit from whatever applied research the councils are asked to undertake. Obviously there is plenty of scope, in such a setting, for research councils to find themselves left high and dry for lack of work.

Now that both documents can be read side by side, it remains a mystery that the government has so stolidly refused to publish the Dainton Report. What it says is what everybody knows it would have said—that there is a case for the doctrine that government departments should continue to sponsor the research in whose applications they have a direct interest, and that the research councils should shoulder more distant responsibilities. With this premise, the notion that the Council for Scientific Policy should be replaced by a stronger body is sensible enough—that step should have been taken years ago, when it first became apparent (in 1967) that the council lacked the power to act and the time to talk. So why has the government risked alienating the research councils and the scientific community by declining to publish the Dainton Report before the Rothschild Report was ready ? The fear that too many people might be publicly committed to the wrong policies can hardly have been serious.

What the government and Lord Rothschild have overlooked is that, for better or worse, the research councils and their constituents (many of whom sit on the 128 advisory committees whose number Lord Rothschild scorns) have been working towards a clubby relationship within which the scientific community has been able to enjoy the sense—or perhaps the illusion—that most decisions were wise and all of them were fair. It will be a great loss if there should now evaporate the research council spirit in which normally sceptical and even suspicious people have been able to trust each other to make disinterested decisions even about the spending of money. The three Christmassy months which the government has now set aside for "wide public debate" will not go far to banish the sense that there is a shotgun solution in the offing (and there is a budget due four months from now).

That said, it is also fair to say that the Dainton Report does not come near to grasping the nettle which has grown up in the past few years about the research councils. Since the Second World War, the budgets for civil science have grown consistently faster than the Gross National Product and all other indices of economic performance. What used to be small and insignificant has grown to be large (a fifth of all public expenditure on research and development is spent by the research councils) and crucial to the health of many branches of national life —university research, for example. Is it any wonder that governments have begun to ask for proof that the research councils can justify their existence and the cost thereof ? It is not so long ago that Sir Solly (now Lord) Zuckerman was advocating the abolition of the research councils on the grounds of demonstrable effeteness. The Dainton Report says that the Council for Scientific Policy undertook the review which it has now completed because of a proposal to transfer the Agricultural Research Council to the Ministry of Agriculture, Fisheries and Food. "The proposal had not previously been discussed with the CSP, who felt that no sufficient case had been made for what appeared to them to be a fundamental and ill-advised change." In the genteel language of government reports, this is fighting talk. It remains an awkward question whether the Dainton Report would ever have provided a sufficient defence of what it calls the research council principle.

A large part of the trouble is that the Dainton Committee has been trying to defend both the research council principle and the details of how it is at present applied. In reality, however, there are a good many places at which the present pattern of research activity could be changed without serious damage. It is, for example, no accident that the Agricultural Research Council should have been the occasion for the Dainton review—quite a large proportion of the research carried out by that estimable body is applied research in the sense that it is intended to be of direct benefit to people such as farmers and those who consume the food they grow. In its time, to its credit, the Agricultural Research Council has been fond of boasting about the way in which its work brought benefits to agriculture. Although a good deal of the council's work is strictly basic research which should not be harmed in any reorganization, it is increasingly hard for the Dainton Committee at this stage to fend off the question why the intended beneficiaries should not have a more direct say in the planning of likely benefits.

It is also hard to see why the Dainton Committee did not put forward more positive proposals for the reorganization of the research councils. To be sure, there is much to be said for providing a framework within which a suitable organization can evolve, but one of the most obvious defects of the system which now exists is that some of the research councils are demonstrably better able to justify a claim on public resources than are others. The Science Research Council has an essential role in higher education, while the Social Science Research Council has an important intellectual job to do in trying to cultivate respectable social science in Britain. Both the Medical and Agricultural Research Councils are divided between basic and applied research, with the basic research less well connected with the universities than it might be, sometimes because the universities play dogs in the manger. The Natural Environment Research Council, by comparison, spans a diversity of interests and objectives which are often indistinguishable from the interests of the other councils. In the circumstances, it would have been a powerful argument in its favour if the Dainton Committee had been able to suggest some of the ways in which the new supervisory board might have set about the removal of some of the anomalies which at present tarnish the research council principle as it is called.

To say all this does not imply that Lord Rothschild's proposals are the only alternative. To be sure, they do ingeniously provide a way in which three of the five research councils can marry basic and applied research, financing the first from what they can wheedle from the Department of Education and Science and the second from the government departments that would act as customers under the new regime. The difficulty, of course, is that nobody can be sure how this would work in practice. Undoubtedly it would be good for the departments if some of the cockiness of the research councils were to rub off in the more sober corridors of what passes for power in the Scientific Civil Service. At the same time, there is a danger that the departments would use the freedom which the Rothschild proposals would give to build up their own research establishments at the expense of perfectly good establishments now in the control of the research councils. Why, for example, should the Ministry of Agriculture pay the Agricultural Research Council for research on plant breeding when it can expand those of its own establishments already active in the field?

A more serious objection to the particular scheme which Lord Rothschild has put forward is that it would tend to institutionalize some parts of the pattern of research within the research councils. The Dainton Committee is, after all, correct in saying that the research council system is flexible and that it could be made more flexible. Once departments are blessed with a block grant for research each year, there is a danger that it will be harder to raise fresh money for applied research in novel fields. But the Rothschild proposals offer no solution to problems such as that posed a week ago by the House of Commons Select Committee on Science and Technology—how best to spend large sums of money on applied research of a kind likely to benefit the computer industry? The failure of the Rothschild Report to deal with questions like this—the questions on which Mr Anthony Wedgwood Benn's green paper foundered two years ago—is one of its most obvious weaknesses. Another is that defence research appears to have been outside the scope of the inquiry.

In the circumstances, it is hard to predict just how the debate will go. The government has endorsed the doctrine of customer and contractor, but that is entirely understandable and in part, at least, something of a formality. Because the future of the Agricultural Research Council is now acknowledged to be the occasion for the present flurry of reorganization, it would be good to think that before the issue is finally decided, it will be more readily apparent how the proposed schemes for reorganization would affect the detailed operation of that research council. Precisely how has Lord Rothschild calculated that £14.5 million of the present budget might be transferred to the Ministry of Agriculture? That is the information needed in the weeks ahead if the wide debate is not going to be a wild sparring match.

It is also important that any new scheme for the administration of civil science should be tried out cautiously. This is a scientific issue, and a few experiments would not be entirely amiss. After all, a good deal of experience would be needed on both sides before the putative customers in the government departments would be able accurately to formulate their demands, and before the contractors in the research councils would be able to respond perceptively. So is it not clear that the first step in implementing Lord Rothschild's scheme should be a carefully controlled attempt to hive off to the Ministry of Agriculture financial responsibility for some (but not all) of the Agricultural Research Council's present responsibilities in applied research? For all their faults—and there are not many—the research councils play too important a part in British scientific life to be dealt with precipitously. But such a change, on a modest scale, would be a useful experiment even for the Daintonites to encourage.

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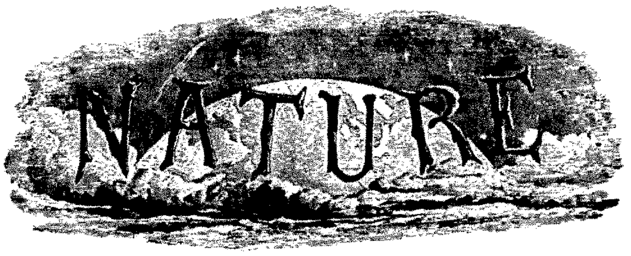
100 Years Ago



M. JOLY, a distinguished member of the French Academy of Medicine, has recently read a paper before that learned society, in which he attributes the enervation of the nation, as evinced during the late war, to the combined effect of alcohol and nicotine upon the national character. "Tobacco," says Dr. Joly, "although of only recent introduction, has gained upon its older rival. Imitativeness and 'moral contagion' have done their work, until the use of this poison has penetrated everywhere—has enslaved the nation, caused personal and racial degeneracy, enervated the entire army, and made it slow to fight and powerless in action. The use both of spirits and tobacco has frightfully increased, and human depravity could scarcely devise a worse compound than the mixture of brandy and tobacco, which is the latest liquid novelty patronised by Parisian sensualists. The French consume more tobacco than any other nation."

From Nature, **5**, 89, *November* 30, 1871

OLD WORLD

EUROPEAN LABORATORY

Italians Show Willing

THE working party set up by the Italian delegation to Esro to make recommendations on the future of the European Space Research Institute (Esrin) has produced a comprehensive plan which will be debated in Paris at an Esro council meeting within the next fortnight. The plan, which is a viable alternative to closing the laboratory, has the added advantage over its predecessor (see *Nature*, **234**, 3; 1971) of having the support of the scientists at Esrin.

The first Italian plan involved splitting the laboratory into an Italian part and a part that would remain under the auspices of Esro, but it is now suggested that there should be cooperation between Esro and the Italian government without a physical division.

According to the new scheme, Italian scientists would be recruited to Esrin but would not exceed 50 per cent of those already employed. The result would be to concentrate Italian research in plasma and space physics and, indeed, under this scheme now put forward, the contribution of the Italian government — through the Centro Nazionale delle Ricerche (CNR)—would come from money saved in the rationalization of their research.

Under this plan, the budget of the reconstituted laboratory would be $2.7 million of which CNR would contribute $1.7 million and Esro the remainder. The property, under this plan, would still be owned by Esro.

Scientists at Esrin seem to be pleased with the plan but, even so, it is clear that the Italian proposal does not meet the original objections to the laboratory —that it carried out research which is incompatible with the present aims of Esro. Financially, the laboratory has been a modest burden—the total Esro scientific budget is $63 million in 1971, but Esrin costs only $2 million a year. Thus the argument that Esrin can still be maintained at a reduced cost to Esro of $1 million does not remove the fundamental objection to the laboratory.

COMPUTER SOCIETY

Expanding into the Red

THE British Computer Society is planning to raise its membership subscriptions (which range at present from £3 for a student to £12 for a fellow) by a "substantial amount" according to Professor A. S. Douglas of the London School of Economics, who was elected president of the society at its recent annual general meeting. The reasons for this are clear from the annual report published in the September issue of *The Computer Bulletin*; the society showed a deficit of £4,608 for the financial year 1970–71 compared with a surplus of £8,950 the previous year. Fortunately the reserve fund stands at about £50,000.

Although the society says that inflation has contributed to the reversal of fortune, it also emphasizes the expansion which has taken place during the past year, including, for example, the equipping and staffing of a print room for the production of the society's ever-increasing output of literature on conferences and computer education. The income from conferences and symposia was only about £2,000 during 1970–71 compared with about £6,000 the year before and this reduction seems to have been due chiefly to a change in the pattern of attendance at the society's marathon Datafair conference—more delegates attended than in 1970 but for shorter periods.

Although membership of the society has increased by more than 10 per cent to about 17,000 since a concerted recruitment campaign was started in May this year, Professor Douglas says that the rate of increase was not as great as had been hoped. About 50 new members a week are now being recruited and the society is aiming for a membership of about 30,000 within two or three years (see *Nature*, **231**, 74; 1971).

University Grants Committee

MRS MARGARET THATCHER, Minister of Education and Science, announced in the House of Commons last week that she was increasing the universities recurrent grant for the 1971–72 academic year from £225 million to £238.1 million. The increase, according to Mrs Thatcher, is to take into account price increases during the past twelve months but Mr Norman Buchan, member for West Renfrew, disputed this as he thought a 6 per cent increase was insufficient to meet the effects of inflation. Mrs Thatcher also added that the provisional grant for the 1972–73 academic year would be £248.5 million, a sum that includes £1.7 million for running the computers which the UGC will take over from the Computer Board for Universities and the research councils. As well as this increased sum for university spending next year Mrs Thatcher announced that she was allocating an extra £23.25 million for equipment.

SPACE

Onward and Upward

A RECOMMENDATION that will be welcomed by the space science community in Britain is that an independent space agency be set up to be responsible to the Minister for Aerospace for all Britain's civil interests in space. This recommendation, made by the Select Committee on Science and Technology in their report published yesterday, will rationalize Britain's space effort which is now divided among several different departments (*United Kingdom Space Activities*, HMSO, £3.15).

The report is the result of a twelve-month effort by the committee that took evidence from people involved in space work in Britain together with evidence from the director-general of Esro and the secretary-general of Eldo. During the time that the committee sat Britain's space programme received setbacks with the scrapping of Black Arrow in July and the failure of the Europa II launcher recently, but there was part compensation, however, in the success of Prospero launched by Black Arrow last month. These ups and downs in Britain's space programme have had little effect on the committee's faith in the future of space activities, and it concludes that the future participation of Britain in space is "inescapable".

"Space should be used wherever necessary or preferable to alternatives as a means to help the broader ends of national policy." The committee feels it is this basic principle that should be followed by Britain, but it recognizes that Britain cannot compete with Russia and the United States. The committee feels that it is the government's duty to ensure that "through national and international space programmes our scientists, engineers and technicians are able to play a full part in advancing the frontiers of knowledge in space and developing their skills in space and its associated technologies".

The committee poses the question of whether Britain should reconsider participation in a European launcher project and so reverse the decision of 1968 when Britain stopped financial support for Eldo. The committee, after reviewing available European launchers, reluctantly concludes, however, that it will be best for Britain to continue its present policy of buying American launchers as required.

In a plea to keep the British space effort at its present level the committee stresses there should be no reduction in British space effort now that Black Arrow has been scrapped. The committee recommends that gaps that are at present evident in the National Space Technology Programme should be filled by the transfer of resources from the defunct Black Arrow project. No worthwhile advances can be made in the development of space vehicles, according to the committee, unless there is a comprehensive research and development effort in the programme.

SCIENCE POLICY

France and Innovation

from *La Recherche*

The Ministry of Industrial and Scientific Research launched a campaign to promote innovation, in Paris, on November 8, with a colloquium on "Innovation and Progress". About a thousand people took part, representing government, industry, universities and think tanks.

The central issue was naturally that of what can be done by the state and entrepreneurs to stimulate the innovative processes. As so often in meetings of this kind, very few really new ideas emerged. It was nevertheless significant that people from all walks of life gathered at an officially sponsored meeting to agree that France is engaged in serious technological competition. They also agreed that France lags considerably in the world technological race, and the various talks, debates and discussions were dominated by the significance of technical and commercial innovation in the process of total competition among industrialized nations. The immediate issues are how best to transform research into development, the role of small and medium enterprise in this process, and the need to create sources of venture capital to assure profitable innovation.

The three-day meeting was also an opportunity for the Ministry of Industrial and Scientific Research to publicize its own moves earlier this year to spur innovation. These measures are chiefly economic and seek to encourage innovation by way of fiscal relief. One of them eases the added-value tax structure at the point of licensing patents for processing and manufacturing techniques. Another smoothes the way for financial corporations which can invest in innovative enterprises by easing the amortization schedules affecting investment capital. There is yet another scheme to establish a public corporation using state funds to finance innovation.

Another goal of the conference was to provide a shop window for the setting up of a National Foundation for Innovation that will be aimed at invigorating research, disseminating information and organizing conferences on innovation.

Until recently, it was fashionable in France to talk about setting up scientific–industrial complexes, but the difficulties encountered recently by such complexes particularly in the United States, together with a lack of enthusiasm on the part of both industry and government in France, have taken the steam out of the concept. Both the government and business now realize that it takes more than good public relations to make this dream come true. Innovation has also been halted by gallic apprehension, as M. Duclos of the Société Montabert reminded his audience, that "Qui dit nouveau en France, dit suspect".

Some participants at the colloquium suggested that it takes more than a well organized meeting such as this to clear all the hurdles and avoid the pitfalls to innovation in a country like France. (Asked about the costs involved in organizing the colloquium, a ministry spokesman would only comment, "C'est très délicat.") Is meaningful innovation really possible in a society whose elite elements linger on, whose government–industry–university establishments will not communicate, and whose institutions remain essentially impervious to the seeping in of external influences? If the meeting had any merit at all, it was that of letting the French research and development world ask itself these very questions.

INDUSTRIAL RELATIONS

Stirring in the Ranks

In spite of assurances to the contrary, the United Kingdom Association of Professional Engineers (UKAPE) is forming a Civil Service Division which hopes to be recognized by the Civil Service Department as the negotiating body for government engineers who are, at present, represented by the Institution of Professional Civil Servants (IPCS). This development springs from the complaint of some civil service engineers about IPCS representation. They claim that technicians are filling professional posts and, by their majority over professionals on committees, are denying the engineers an effective voice. As a result Mr Kenneth Peplow, general secretary of UKAPE, approached IPCS last year and suggested an affiliation between the two to give the engineers a stronger voice. When the proposal was rejected, the UKAPE formed its Civil Service Division in spite of the statement by Mr Peplow during negotiations that his association "would not try to usurp in any way the negotiation arrangements of your association".

Mr C. Cooper, deputy general secretary of IPCS, said this week that there is no basis for the complaints. He said that the engineers are part of the works group, which includes architects and surveyors, and are represented by a professional staffs committee—which has said that there is no place for UKAPE in the civil service.

Mr E. Pallant, the national organizer of UKAPE's civil service division, said last week that the division was formed as the result of pressure from within the civil service rather than from the association's headquarters. He thinks that once the division is recognized by the Civil Service Department eighty per cent of engineers will join the association. As things stand, only some fifteen out of the 10,000 government engineers are committed to the division, but recruitment is due to start in the next few days. If sufficient numbers support the association it will apply for recognition to the Civil Service Department and, if it is refused, to the Industrial Court for a ballot under the Industrial Relations Act which could force the department—and IPCS—to recognize the division.

Mr Cooper describes this plan as "impossible" and says that if UKAPE thinks it will work "they are living in fairyland" as IPCS already represents engineers effectively and has a membership of 80 per cent among government engineers. Mr Cooper does not deny that engineers have problems over pay and careers but he hopes to see progress made when the new negotiations begin on January 1 next year—when IPCS, not the division, will be representing the engineers. Mr Cooper said that there are no doubt a few dissidents but there is no mass movement of engineers to UKAPE. "Their cause will not be advanced by dissipating their efforts," says Mr Cooper, "and the last thing we want is recruitment wars."

COMPUTERS

All Things to All Men

Although computer companies in Britain have reacted favourably to the Select Committee on Science and Technology's report on prospects for the British computer industry, there have

Royal Society Medals

The three Royal Medals of the Royal Society for 1971 have been awarded to Dr G. Herzberg, National Research Council of Canada, for his "distinguished experimental researches in atomic and molecular spectroscopy and its applications in chemistry, physics and astronomy", to Dr M. F. Perutz, Medical Research Council Laboratory of Molecular Biology, for "pioneering work on the molecular biology and structure of proteins" and to Dr P. E. Kent, British Petroleum Company Ltd, for "distinguished contributions to oil and gas explorations and the geology of oil and gas fields".

been some misgivings about the criteria for purchase preference that have been proposed (see *Nature*, **234**, 117; 1971).

Sir John Wall, chairman of ICL, said this week that the report was a valuable contribution to the computer debate. He also pointed out that the Select Committee's "overall recommendations that imaginative support and preference should be given by the government to computer suppliers whose controlling interest is held by British nationals echo government policy expressed by Mr Frederick Corfield at the end of July 1971". ICL, he added, is well placed to meet the criteria proposed as a guide to purchasing preference.

Obviously hoping that the Computer Purchasing Board, if it is set up, would be able to interpret the purchasing criteria flexibly, Mr E. R. Nixon, managing director of IBM (UK) Ltd, said that he welcomes any proposals to increase competition for public sector business. "With two major manufacturing plants and a large development laboratory in Britain, IBM (UK) Ltd is, of course, already making a considerable contribution to the economy and, with its world wide experience of advanced applications to draw on, it is well placed to make a major contribution to the government's future needs." The sales of IBM (UK) Ltd were £170 million in 1970 compared with £131 million for ICL.

A spokesman for Honeywell was more critical of the report although he generally welcomed it and considered that it made some reasonable and firm proposals. Honeywell's chief complaint was that some of the recommendations in the report were incompatible with others. In particular it was not clear how the call for an end to the system of granting a single contract for a total system to one hardware manufacturer could be reconciled with, for example, the recommendation that preference should be given to suppliers whose controlling interest is held by British nationals—thus effectively ruling out all companies but ICL. The proposal to establish a Computer Purchasing Board has, however, met with Honeywell's approval on the grounds that the computer industry would then be dealing with the government through a single body. The proposal, Honeywell says, augurs well for greater consistency of treatment in the future and for a better understanding between the government and the computing industry. On the other hand, the company feels that the report does not spell out in sufficient detail how the recommended research and development support of £50 million should be distributed among British computer manufacturers; but it does consider that the setting up of a Computer Research and Development Board would greatly assist efforts to promote common standards, both in hardware and software.

REPRODUCTIVE BIOLOGY

WHO convenes Advisory Group

THE first meeting of the advisory group which is to help to direct the Expanded Programme of the World Health Organization on research, development and training in human reproduction was held in Geneva from November 22 to 26 (see *Nature New Biology*, **234**, 3; 1971). Invitations to attend the meeting were issued to: Dr B. Rexed, Public Health Services, Stockholm; Professor B. K. Adadevoh, University of Ibadan; Dr Lidija Andolšek, University Teaching Hospital for Obstetrics and Gynaecology, Ljubljana; Professeur Etienne Baulieu, Faculté de Médecine de Bicêtre, Paris; Professor Jack C. Caldwell, Australian National University; Dr Philip A. Corfman, National Institute of Child Health and Human Development; Professor Elsimar Coutinho, Universidade Federal da Bahia, Salvador; Dr A. B. Kar, Central Drug Research Institute, Lucknow; Dr Anne McLaren, Institute of Animal Genetics, Edinburgh; Professor William Paul, Toronto Western Hospital, Toronto; Dr Sheldon Segal, Rockefeller University; and Professor N. A. Yudaev, Academy of Medical Sciences of the USSR, Moscow.

GEOLOGY

Abstracts Abandoned

GEOLOGISTS are concerned that the decision of the United States Geological Survey to end publication of *Abstracts of North American Geology* and *Geophysical Abstracts* next January will leave them without an effective and comprehensive English language abstracting journal. The decision seems to have been taken to avoid duplication of service, but the *Bibliography and Index of Geology* published by the Geological Society of America is not, according to Professor K. Clayton, University of East Anglia, an effective substitute for the doomed journals as it carries citations and key words but no abstracts. It also costs $250 a year compared with $10 a year for *Abstracts of North American Geology*.

There is at least some compensation for the geologists in that next January *Bibliographie des Sciences de la Terre* and the geology parts of *Bulletin Signalétique* will be combined to provide an expanded titles and key words service. There are also plans for the reconstituted journal to have input from the German government and from some East European countries. It is possible that some time in the future the Institute of Geological Sciences in Britain could provide a contribution but there are no plans at present to extend the journal to give a full abstracting service.

Next year there will be three chief English language abstracting journals that cover geology. *Mineralogical Abstracts* covers the fields of mineralogy, geochemistry and petrology, edited by Dr R. A. Howie of King's College London, and claims a 50 per cent coverage of all publications but a 90 per cent coverage of significant articles. There will also be two volumes available in the Geographical Abstracts series—*Geomorphology* and a new volume *Sedimentology*. Between them these journals only cover a part of the field and several important areas will not be abstracted effectively after the final publication the United States Geological Survey journals.

CHEMICAL INFORMATION

New Service Planned

THE United Kingdom Chemical Information Service (UKCIS) and the Institute for Scientific Information (ISI) are launching a new information service based on magnetic tapes which store data on the structure of new chemical compounds reported in the literature. The tapes are prepared each month by ISI but the service will be administered by UKCIS which is operated at the University of Nottingham by the Chemical Society. The existing facilities to subscribers offered by UKCIS depend upon data tapes compiled by the Chemical Abstract Service, which is partly financed by the American Chemical Society.

Each of the ISI monthly tapes contains data on about 12,500 new compounds, encoded in such a way that letters and numbers correspond to particular sub-structures (for example carbonyl and hydroxyl groups); this makes it possible for searches to be made for chemical sub-structures of particular interest to individual subscribers while also allowing recognition of overall structures.

Subscribers to the new service will receive monthly lists of relevant compounds, each associated with an abstract in the ISI publication *Current Abstracts of Chemistry*, which details references synthesis routes and so on. The cos to subscribers will probably b between £70 and £120 a year, abou the same as for the other services whic are to continue as before.

NEW WORLD

How Far will this Special Action Office Go?

PRESIDENT NIXON'S campaign against drug abuse, launched in his message to Congress in June this year, has become bogged down in congressional committees. Last week, the Senate Committee on Government Operations reported out a bill that differs in some important respects from Nixon's original intentions. The bill now goes to the Senate Committee on Labor and Public Welfare which also has an interest in its provisions. Meanwhile, in the House of Representatives, the Subcommittee on Public Health and Environment of the Committee on Interstate and Foreign Commerce is in the throes of marking up legislation after conducting exhaustive hearings on the bill. What was expected to be a quick passage through Congress has therefore become a long drawn out process, but both the White House and key congressmen involved in the legislation are confident that a bill will soon be ready for the President's signature.

In some respects, the delay in presenting the bill to the floor of the House and the Senate reflects the complicated nature of the differing philosophies over how to attack the problem of drug addiction. The nub of President Nixon's original proposal was the creation of a Special Action Office on Drug Abuse and Control within the Executive Office. The office would be responsible for directing federal efforts to rehabilitate drug addicts and directing programmes aimed at education on drug abuse. An important criterion was that the Special Action Office should not be concerned with law enforcement, since rehabilitation should be treated separately from the question of legal sanctions against drug users and pushers.

The Senate Government Operations Committee last week reported out a bill that extended the scope of the Special Action Office but clipped its powers. Essentially, the committee seeks to give the office the power to recommend to the President policies for the Bureau of Narcotics and Dangerous Drugs (part of the Department of Justice) but takes away from the director of the office the power to control and carry out programmes directly from the White House and to transfer money from one agency to another. In the original bill, President Nixon had given the office the power to regulate the budgets of the various federal agencies that are devoted to drug rehabilitation and education, but the committee decided that his powers should be limited to providing overall policy direction of federal efforts in drug control with the power to modify budgets. The director would not, however, be able to take over the direction of individual projects.

Another important change put in by the committee is that the Special Action Office should have some limited direction over law enforcement and related activities. The direction would in fact boil down merely to the offering of advice. The House Subcommittee on Public Health and Environment is now likely to report a similar bill to the main committee in spite of the conviction held by some members that the powers of the Special Action Office would not be addressed to one of the most important points—the international regulation of poppy growing and the smuggling into the USA supplies of heroin.

MARINER 9

First Results May Aid Russian Lander

As expected, the safe arrival of Mariner 9 in orbit around Mars (see *Nature*, **234**, 67; 1971) has provided accurate data on the orbit of the planet and its gravitational field. These discoveries have provided the first opportunity for practical cooperation between the American team controlling Mariner 9 and the Russians guiding the progress of their probes Mars 2 and Mars 3.

On November 19 the following findings were announced from the Jet Propulsion Laboratory in California, control centre for the mission:

- A large bulge at the equator of Mars
- Gravitational anomalies which may be caused by martian mascons
- Water vapour present in the atmosphere over the south pole
- Surface temperatures ranging from 240 K at mid-afternoon to 200 K at night
- Uniform atmospheric temperature of 350 K from near the surface to a height of 40 km

In addition, the dust storm clouding the martian surface now appears to be clearing and surface features should soon be identifiable.

It seems that improved figures for the exact orbit and ephemeris of Mars have already been relayed to the Russians. These refine standard measurements by only a few kilometres, but the detailed information which is being gathered about the martian mascons could prove extremely valuable when the Russian probes come to attempt the soft landing which has been unofficially promised. Variations in the orbit of Mariner 9 caused by local irregularities in the planet and by the large equatorial bulge cause changes in the craft's velocity of 2 to 3 millimetres per second, and produced an average 5 second change in the duration of its orbit during each of the first 8 revolutions. This slowing down by 40 s should be regained as Mariner 9 shifts away from the direct influence of the bulge, according to Dr W. O'Neill of the Jet Propulsion Laboratory.

The insertion of the spacecraft into orbit went smoothly, and required rather less fuel than had been allowed. The manoeuvre, which changed the orbit of the spacecraft so that periapsis (closest approach to Mars) is now 868 miles and takes place in the middle of the viewing period available to the Goldstone antenna tracking Mariner 9, left plenty of fuel for subsequent trim manoeuvres using the main engine, which is rated at 300 lb thrust but appears to be performing rather more efficiently.

Just how severely the strong winds seen whipping up the present dust storm on Mars might affect a soft landing can only be determined effectively by making a landing attempt. It does seem certain, however, that the Russians will wait for the storms to clear as much as possible before venturing such a step. Traditional Soviet secrecy makes it impossible to say just what is planned, but it is known that the NASA Viking lander, scheduled for 1974, will be able to wait for up to one month in Mars orbit if conditions are not immediately suitable for a landing on its arrival. With the Russian lander in prospect and Mariner 9 now in full scientific operation after orbital adjustments, the weeks ahead seem likely to produce the hoped for excitement after the necessary tedium of the long interplanetary journey.

SCIENCE POLICY

Two Views of British Science

THE British Government has at last published the report of the Dainton Committee and, for good and unexpected measure, the frequently conflicting report on the same subject which has been prepared by Lord Rothschild, the head of the Central Policy Review Staff (Cmnd. 4814, HMSO, £0.525).

The two documents appear within the same green cover, and the government says that although it endorses the principle laid down by Lord Rothschild that the relationship between government and the research councils should in future resemble that between customers and contractors, it says that it will not make detailed decisions about the proposed reorganization until there has been "wide public debate". The intention is that formal discussions with interested bodies such as the Royal Society should be completed by February 29 next year, but interested persons are invited to send their views to the Chief Scientific Adviser at the Cabinet Office before January 14.

The Rothschild report is a provocative document written in a kind of racy telegraphese. Its starting point is the view that there is no meaningful way of striking a correct money balance between pure and applied research. And in the proper organization of applied research, "the customer says what he wants, the contractor does it (if he can) and the customer pays".

Organizing the Customers

Although it is acknowledged as sensible that the Department of Education and Science should support basic research through the research councils and the University Grants Committee, Lord Rothschild complains that much of the research sponsored by the Agricultural, Medical and Natural Environment Research Councils is applied research, "with no customer to commission and approve it. This is wrong. However distinguished, intelligent and practical scientists may be, they cannot be so well qualified to decide what the needs of the nation are, and their priorities, as those responsible for ensuring that those needs are met."

In the context of government science, the customers are government departments. To enable them to decide which research and development programmes are necessary and how much should be spent on them, the customers will need a Chief Scientist to formulate needs and a "Controller R & D" to administer the programme. In practice, the argument goes, it would be necessary to provide the officials concerned—who would work in parallel with each other—with staffs big enough to do the work required. The Rothschild report suggests that there should be a strict separation of capital and current expenditure on research and development.

Research Surcharge

One of the most novel proposals in the report is that it should be openly acknowledged that something like 10 per cent of the cost of applied research is at present properly spent on more basic work. Under the proposed arrangements between customers and contractors (the research councils and other government research establishments) there should be a "general research surcharge". The total amount available under this heading on the basis of current budgets would amount to no less that £54 million a year.

The Rothschild report's appraisal of the research councils is sceptical, to say the least. At the outset, the report raises the question whether it needs more than 1000 people, with salaries which exceed £4 million a year, and 128 advisory committees, to spend a total of £109 million (in the current financial year). "A review of these numbers is needed."

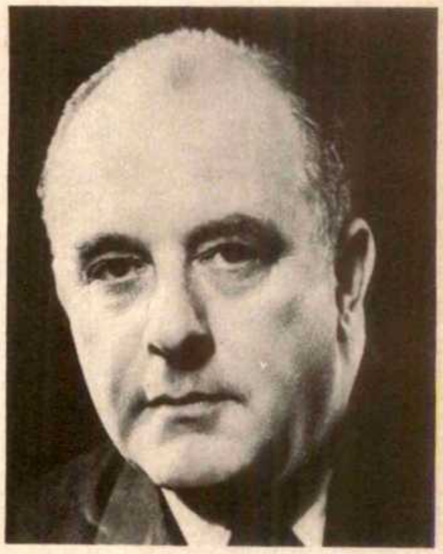
Lord Rothschild explains that the Science Research Council has been excluded from his review because only a little of the work it sponsors is applied research and that the Social Science Research Council has been excluded "because it is in its infancy". There has plainly been some dispute about the distinction between pure and applied research. Lord Rothschild says that the Council for Scientific Policy does not accept that there is an "unambiguous" distinction (in the sense of whether or not there is a customer), and goes on to ask that the government should "reject the view that there is no logical division between pure and applied research, a view that may be intended to protect the research councils from the imaginary ravages of applied R & D users."

Department Satellites

With these reservations, Lord Rothschild would like to see the heads of the Agricultural Research Council (ARC), Medical Research Council (MRC) and Natural Environment Research Council (NERC) become the controllers of R & D for the appropriate government departments—the Ministry of Agriculture, Fisheries and Food, the Department of Health and Social Security and (for NERC) the Department of Trade and Industry and the Department of the Environment.

For practical purposes, the result

Sir Frederick Dainton



Lord Rothschild

would be that the three research councils would become satellites of one or more government departments. "The present division is both illogical and undesirable. It perpetuates meaningless or harmful distinctions between research and development, and panders to scientific snobbery—the 'haves' in the research councils and the 'have-nots' in the departments." The report suggests that each research council should have a whole-time chief executive and a part-time chairman.

Financing the Changes

Where will the money come from to support these activities? The nub of the recommendations is that a substantial part of the budgets of the three research councils under scrutiny should be transferred from the Department of Education and Science to the appropriate customer department. Numerically, something like £26.7 million out of the current budget for the research councils of £109 million should be reallocated in this way. The exact amounts are shown in the table below.

What assurance could there be that the departments would not take their new-found money for research and development and place contracts with organizations other than the research councils? For the first four years, Lord Rothschild would impose some restrictions on the extent to which departments would be free to redeploy their resources. In the first year, there could be no reduction of the amount of business finding its way into a research council's hands, and in the succeeding years the amount could not be reduced by more than 10 per cent each year. "It is naturally for the departments to decide if they wish to increase their payments to the research councils".

Some of the salt which Lord Rothschild has rubbed into people's skin, wounded or otherwise, lies in the recommendations which he has to make about the Council for Scientific Policy. This, he says, should be reconstituted in such a way that the five chief executives of the research councils should be *ex officio* members, together with the chairman of the University Grants Committee, and that there should also be four independent scientists and a part-time chairman blessed by the president of the Royal Society. The chief function of the CSP should be to advise on the division of funds for the research councils which are not in the gift of customer departments. There is some dispute between Rothschild and Dainton (see below) on whether the president of the Royal Society should automatically be a member—Rothschild thinks not.

Lord Rothschild also flatly rejects the distinction between tactical, strategic and basic research which is the starting point for the Dainton analysis. On strategic science, "work of general practical interest", the Rothschild report says that the names of the research councils "imply applications"—and that the philosophy of the Dainton report "should be rejected".

Lord Rothschild asks that the research councils should re-examine their policies of setting up research units around individual scientists and then of feeling free to close them down again if the person concerned should die, retire or move. On the need for long-term research, the report says that both the universities and the general research surcharge should help to make sure that departments do not sacrifice everything to immediate objectives, while it should be in the brief of government research administrators that variety is a necessary part of a healthy research programme. But with this reservation, "longer term research has no special merit or value in itself, and there is no positive correlation between the importance of a discovery and the time it took to make".

Price of Advice

The Rothschild report also has several detailed recommendations about the organization of the government's relations with the scientific community. It suggests that the British Government's annual subvention to the Royal Society should be paid by the Cabinet Office rather than by the Department of Education and Science. Lord Rothschild would like to see a rationalization of the payments made to the members of the research councils and the other scientific advisory bodies—the implication is that the £15.75 a day paid to independent members of the Council for Scientific Policy, and the £750 a year paid to the independent members of the Medical Research Council, is more than the same people would be paid for attending scientific advisory meetings elsewhere in government. "It is strongly recommended that this subject be examined or re-examined by the Civil Service Department, attention being paid to the duty of the citizen to render public service and to be remunerated with this in mind."

Lord Rothschild has strong things to say about the need for more mobility between the scientific civil service and the rest of it. He deplores the meagre transfer from scientific to administrative posts, argues that movement through a laboratory is necessary for the maintenance of its scientific quality, and suggests that a start should be made "in the rectification of this organizational failure" by giving putative heads of government laboratories at least one year's experience in the administrative branches of the civil service.

The Chief Scientific Adviser to the British Government should, according to the report, provide himself with at least one biologist and one chemist within his present complement of four physicists, two mathematicians, one engineer and one economist. His function should be to warn departments of occasions when the research programme of one may have a bearing on that of another but, in this world in which the customer is supreme, there is no case for asking that the Chief Scientific Adviser should exercise a supervisory function.

Lord Rothschild does not so much reject the Haldane principle as reinterpret it. He says that the doctrine "is sometimes invoked to justify the independence of applied scientists from those who may benefit from the results of their work". He then provides a list of contradictory quotations from the report and concludes that the most commonly quoted form of the Haldane principle has "little or no bearing on the conduct and management of government R and D in the 1970s".

Dainton's Deliberations

The Dainton report begins with the acknowledgment that governments spend money on science only because they are "aware of the power of science to serve national goals". Avoiding the trap of classifying scientific work into "pure" and "applied", the committee distinguishes between three categories of research—tactical, strategic and basic. Basic research, in this definition, is intended as research and training with "no specific application" in view. Strategic research is the foundation for the day-to-day needs of government and industry for research and development. Like all

Reallocation of Research Council Budgets

Council	Present budget (£ million)	Transferred to department(s) (£ million)
SRC	50.9	0
SSRC	2.2	0
ARC	18.7	14.5
MRC	22.4	5.6
NERC	15.3	7·6
	£109.5 million	£27.7 million

previous lexicographers of science, the Dainton committee emphasizes the fuzziness of the boundaries between the three categories of science.

Most of the committee's work is concerned with the research councils which are at present the chief sources of funds for the support of civil science in Britain and the report says that it has deliberately set out to re-examine the old Haldane doctrine—the notion that research is most fruitfully applied to the needs of government when the agency responsible for research is separate from the government department most directly concerned. Although the report does little more than say that it is now necessary that there should be close links between policy formation and research, the fact that the committee has not endorsed the Haldane doctrine is in itself a sharp break with the precedents of previous committees on the administration of civil science in Britain. In the end, however, the committee comes out with what it calls a reaffirmation of the research council principle—to allocate the research councils to the departments which they might seem to belong would be inefficient and uneconomic.

The Dainton committee is, however, strong on the need for closer links between the research councils. On questions such as the balance of effort in civil science, the breaking of new and interdisciplinary ground as with pollution research and the organization of studies of scientific manpower, the committee considers that there needs to be closer coordination than in the past. At the same time, it says that it is improbable that the Council of Scientific Policy, which is an advisory organization, could be strengthened sufficiently to fill the bill.

For all these reasons, the committee says, there is a need for important changes in the present method of organization. The chief need is that government departments should play a fuller part in the formation of scientific policy. "The principles of scientific responsibility and of judgment of scientific merit which are important characteristics of the research council system must, however, be preserved".

The committee mentions but rejects the proposal, much talked of in the past few months, that there should be a single research council responsible for the administration of all government subventions for civil science—such an organization would be too remote and too prone to error. Rather, the committee wishes to make the most of the sense of involvement with the formulation of scientific policy which, it says, is provided by the committee system under which the research councils operate at present.

This is why the committee comes out with the proposal that there should be a coordinating board consisting of the heads of the existing research councils which would be able to act as the direct intermediary between the Department of Education and Science and the research councils themselves. The board would naturally become, according to the Dainton committee, the chief source of scientific advice to the Department of Education and Science, and would in particular be responsible for settling such boundary disputes between the research councils as might arise. The committee suggests that the coordinating board should also be empowered to "add to or subtract from the number of research councils in response, for example, to the growth of new disciplines and the emergence of new professional groups. It should not, however, at any stage so reduce the number of research councils that the virtues of the specialist council were lost". This passage will be scanned with close attention by all those who may wish to use the publication of this report as an argument in favour of the abolition or the retention of one or other of the research councils—the Agricultural and the Natural Environment Research Councils have been most at risk.

How will the new system make it possible for government departments other than the Department of Education and Science to have their say about the formulation of policy on research in the civil field? The suggestion is that the coordinating board should include as full members representatives of the departments most likely to be interested. "So as not to make the board too big," the committee suggests that the Cabinet Office should be represented, together with three other departments chosen in rotation. An important feature of this recommendation is that there should be independent members among whom the president of the Royal Society would be appointed as of right. The chairman of the University Grants Committee and at least one vice-chancellor should also be appointed.

The report says that the chairman of the coördinating board would be the key figure in the new arrangement, but that the board would also have to be provided with a secretariat sufficiently strong to shoulder a good deal of planning and administration. Within this framework, the Dainton committee seems to be in favour of a limited amount of reorganization of responsibility. It says that some of the work at present carried out by research councils could be transferred to an appropriate government department. On the other hand, it would like to see the new board assume responsibility for some departmental function such as the British Museum (Natural History) (at present under the direct control of the Department of Education and Science).

In short, the Dainton report turns out to be not so much a recipe for change as for a framework within which change might happen.

Table 1 Research and Development in Britain, 1961–1971

Sector providing funds	1961–62		1964–65		1967–68		1970–71 (estimates*)	
Government support	£ million	Percentage of (4)	£ million	Percentage of (4)	£ million	Percentage of (4)	£ million	Percentage of (4)
(1) Total civil	139.3	36.2	171.9	40.3	259.4	53.5	350.0	60.3
(2) "Research council" element in (1)	24.0	6.2	38.0	8.9	57.1	11.8	93.8	16.2
(3) Total defence	245.7	63.8	255.1	59.7	225.9	46.5	230.0	39.7
(4) Total civil and defence	385.0	100.0	427.0	100.0	485.3	100.0	580.0	100.0
	£ million	Percentage of (10)	£ million	Percentage of (10)	£ million	Percentage of (10)	£ million	Percentage of (10)
(5) Total civil and defence as returned by sectors carrying out the work	378.2	57.5	421.2	54.6	493.1	51.3	n/a	—
(6) Universities (own funds)	1.3	0.2	1.8	0.2	5.7	0.6	n/a	—
(7) Private industry and public corporations (including research associations)	266.2	40.5	311.6	40.4	405.2	42.1	n/a	—
(8) Funds from overseas	12.0	1.8	20.8	2.7	30.3	3.1	n/a	—
(9) Other			16.0	2.1	27.8	2.9	n/a	—
(10) Total	657.7	100.0	771.4	100.0	962.1	100.0	n/a	—

* Figures in this column include expenditure overseas (estimated to total £40 million).

NEWS AND VIEWS

Gravitational Lenses and the Structure of the Universe

THERE are several possible ways of explaining the redshift of the emission lines observed in the spectra of quasars. The most obvious view, and the one that is most widely accepted, is that quasars are at cosmological distances, and that their redshifts are due to the expansion of the universe itself. Given the present values for the Hubble constant, H, and for the mean density, $\bar{\rho}$, of matter in the universe, one can then calculate the distances, L, to the various quasars. Admittedly there are uncertainties in H, and even more so in $\bar{\rho}$, and these introduce corresponding errors into the estimates for L. But in all cases it is found that the quasars are extremely distant objects, and that therefore they must emit energy at a prodigious rate. A luminosity of 10^{47} erg/s^{-1} would be quite typical for a quasar; this is $\sim 10^4$ times larger than the combined luminosities of all the stars in a normal spiral galaxy.

The alternative explanations for the quasar observations seem, at first sight, to avoid this conclusion and would save us from having to admit that such powerful sources of radiation exist. They fall into three categories and the alternative postulates are, first, that the quasars are not at cosmological distances but originated quite close to the galaxy in an explosive event which gave them their high velocities; second, that the redshift is gravitational and not due to the Doppler effect; and, third, that the redshift is cosmological but that the quasars are much less luminous than they appear to be. According to this theory their true brightness is overestimated because gravitational lenses in the intervening space have to some extent focused their radiation onto the Earth.

None of these alternative explanations has been very successful. The local theory puts us in an unacceptable, almost pre-Copernican position with respect to the rest of the universe for the Earth should have to be right in the middle of an expanding association of some 300 or more "quasars". But where are the corresponding associations surrounding at least some of the other galaxies? Surely some at least of the "quasars" belonging to these associations would have to be approaching the Earth, and would therefore have to be blueshifted. No such object has ever been found, a significant null result.

The second postulate, the gravitational theory, suffers from the drawback that it is hard to concentrate sufficiently a large enough mass to produce the necessary redshift. Masses can be suitably distributed to bring about such redshifts, but not for long. In general they are endangered by gravitational instabilities, with the consequent loss of the quasar into a black hole.

The only one of the alternatives left is therefore the gravitational lens theory. At first sight this seems to be the most improbable theory of all; indeed, just what is a gravitational lens? From relativity theory it is known that the presence of matter distorts the geometry of space. Radiation therefore does not travel in straight lines in the Euclidean sense. Any cosmological model is based on a geometry which allows for this effect, at least as far as the smoothed-out density distribution of mass in the universe is concerned. But this is not quite enough. Much of the matter in the universe is lumpy, rather than smooth, and is concentrated into various hierarchies of condensations like galaxies, star clusters and stars. The radiation passing through or close to a condensation is deflected more than the average for the universe. The effect is analogous to refraction in optics; hence the term gravitational lens.

On page 199 of this issue of *Nature*, N. Sanitt assesses the importance of the gravitational lens effect on the radiation from distant sources. He discusses, in particular, what happens when the radiation travels past a model galaxy with suitably symmetrical properties. He then calculates the probability that an observer on the far side sees an image, intensified by a factor A, or more. Given a large enough value for A, say 10^3, even a relatively modest source like the nucleus of a Seyfert galaxy might be mistaken for a quasar. The redshift of the spectral lines is, of course, unaffected by the focusing process.

Characteristically there is a probability proportional to A^{-2} that a gravitational lens would produce a magnification A, or larger. Other factors also enter the expression for the probability and it is assumed that there is no correlation between the positions of the source, the lens and the observer. But the theory has got off to a bad start, for one can only expect that, at best, one Seyfert in a million, with luminosity 10^{44} erg s^{-1}, will mimic a quasar the luminosity of which is a thousand times (or more) as great. What is known about the statistics of Seyferts argues strongly against the existence of an adequate number to account for all the quasars. So it is concluded that the straightforward interpretation was right, and that most quasars are really as bright as they appear to be.

At this stage should the study of gravitational lenses be regarded as a waste of time? To answer this, Sanitt's result must be reconsidered, and in particular the distribution of probabilities for magnification by a factor larger than A. The inverse square dependence that he finds is quite generally valid: it would equally well occur for a radiation field that had become distorted by encounters with a random distribution or arbitrarily shaped masses in the universe. The only proviso is that the source of the radiation must be sufficiently redshifted; gravitational lenses tend to have a large focal length and there is no important focusing effect for nearby objects. But gravitational distortions are bound to set in for sources beyond a certain distance and it is entirely possible that some of the quasars are far enough away.

Very large magnifications will still occur only rarely but it is profitable to discuss the influence of smaller changes. Small magnifications or demagnifications are far more likely to occur and may well confuse the statistics for the luminosities of distant compact sources. Just how much gravitational distortion occurs will depend on the total mass of the various condensations. The present inventory of the mass distribution in the universe is not complete enough to give a good estimate. In fact, there is much talk of "missing mass", for example in connexion with the problem of the equilibrium of clusters of galaxies. In principle the gravitational lens effect provides a probe for detecting the various condensations of masses. It may yet turn out to be a very useful concept with interesting applications.

This experience with quasars leads to several more general conclusions. The first is that one must occasionally accept the commonsense interpretations of striking observational results, even if they trample on cherished theories. The second is that quite often a theoretical study, undertaken for the wrong reasons, may turn out to be much more useful in unexpected ways. But most important it shows how science, like most other human activities, proceeds by trial and error.

Further Progress in Cholinergic Receptor Studies

SINCE the snake venom toxin α-bungarotoxin was reported to be a unique tool for the investigation of cholinergic receptor sites because of the highly specific manner in which it binds to such sites (Changeux *et al.*, *Proc. US Nat. Acad. Sci.*, **67**, 1241 ; 1970 ; Miledi *et al.*, *Nature*, **229**, 557 ; 1971), progress in this field has been rapid. Miledi and Potter (*Nature*, **233**, 599 ; 1971) last month reported the use of α-bungarotoxin in studies of cholinergic receptor sites in vertebrate muscle, and on page 207 of this issue of *Nature*, Barnard, Wieckowski and Chiu report the results of studies similar to those of Miledi and Potter, performed at the same time.

Barnard *et al.* used α-bungarotoxin which was radioactively labelled by acetylation with tritium labelled acetic anhydride. The labelling procedure was shown to have no effect on the pharmacological potency of the toxin in blocking acetylcholine effects at muscle cholinergic receptors. When labelled toxin was administered to mice or if diaphragm preparations were incubated *in vitro* a complete block in neuromuscular transmission resulted. The irreversible blocking effects of bungarotoxin were prevented if the reversible antagonist *d*-tubocurarine was present during exposure to toxin. The binding of labelled toxin to nerve-muscle preparations was also resistant to removal by repeated washings.

In preparations saturated with labelled toxin, autoradiographic studies showed a highly selective localization of the radioactivity over neuromuscular end-plates on the muscle surface. Quantitative autoradiography of end-plates labelled with bungarotoxin, or with the irreversible acetylcholinesterase inhibitor di-isopropylfluorophosphate (tritium labelled), showed that the densities of toxin binding sites and acetylcholinesterase active sites on the end-plate membrane were equal. These two types of binding site were shown to be independent, because there was no mutual inhibition of binding by the two labelling agents used if both were present together. The number of cholinesterase sites and toxin binding sites were equal, so that estimates of the number of toxin binding sites were made by β-track counting of end-plates labelled with ^{32}P-DFP. This gave values of 3.0×10^7 sites per end-plate in mouse diaphragm muscle, and values between 3 and 9×10^7 sites per end-plate in other mouse and chicken muscles. The value for mouse diaphragm is similar to the value of 1.6×10^7 bungarotoxin binding sites per end-plate reported recently by Miledi and Potter. Barnard *et al.* calculate that the density of toxin binding sites (that is to say, cholinergic receptors) on end-plate membranes is 12,000 per μm^2, and the receptor sites and cholinesterase active sites together occur at a density of 1 protein subunit per 5,000 Å^2 of membrane. This suggests that the enzyme and receptor molecules may be present as a fairly tightly packed mosaic in the end-plate membrane.

Barnard *et al.* have also estimated, by comparison of the time course of blockade of neuromuscular transmission and the time course of toxin binding to muscle, the proportion of receptor sites which must be blocked before any pharmacological blockade is observed. They show that no impairment of neuromuscular transmission occurred if about 50 per cent of the toxin binding sites were occupied by bungarotoxin, and that blockade thereafter became marked when about 70 per cent of the toxin sites were occupied. This suggests that the "spare receptor" population at mouse diaphragm end-plates may be considerably less than was suggested by the calculations of Miledi and Potter.

The identity in number of cholinergic receptor sites and acetylcholinesterase active sites reported by Barnard *et al.* in mammalian muscle has also been described in the electric organs of electric fish (Miledi *et al.*, 1971) and in electric eels (Changeux *et al.*, 1970). The significance of this stoichiometry in functional terms is not clear, but it may have important implications for the question of the origin of the esterase and receptor sites at neuromuscular junctions and at other cholinergic synapses. It has recently been suggested (Hall and Kelly, *Nature New Biology*, **232**, 62 ; 1971 ; Betz and Sackman, *Nature New Biology*, **232**, 94 ; 1971), that acetylcholinesterase may not be located in the muscle membrane, but rather in the basement membrane overlying the muscle surface. The identity of receptor sites with enzyme sites suggests, however, that the two macromolecules involved probably have a common biosynthetic origin, presumably within the muscle cells.

Further important progress in the characterization and isolation of cholinergic receptor sites is reported by Changeux, Meunier and Hutchet (*Mol. Pharmacol.*, **7**, 538 ; 1971), who worked with the cholinergic receptors in the electric organ of the eel, *Electrophorus electricus*. The snake venom toxins α-bungarotoxin, and the α-toxin of *Naja nicricollis* (a cobra venom with properties similar to those of bungarotoxin), were used as specific receptor binding agents, and were found to prevent the reversible binding of radioactively labelled decamethonium to electroplax membranes, and to solubilized preparations of these membranes made by treatment with deoxycholate. The use of equilibrium dialysis binding of a reversible agonist, decamethonium, as a method for detecting cholinergic receptor sites has certain advantages over the use of the irreversibly binding venom toxins. In the final analysis, receptor purification must make use of marker molecules which can easily be removed from the purified preparations—this is not the case with α-bungarotoxin which binds very strongly to the receptor sites.

Changeux *et al.* were also able to measure in a series of elegant kinetic experiments the binding constants for the affinity of binding of agonists such as decamethonium and carbamylcholine, and antagonists such as *d*-tubocurarine, gallamine and the venom toxins. These studies establish the important point that the constants for the binding of agonists and antagonists in the solubilized receptor preparations are similar to those measured indirectly from pharmacological dose response curves in the intact electroplax, that is to say, that the receptor sites have not undergone any fundamental change in their properties during the extraction procedure. Changeux and his colleagues also report preliminary results on the use of venom toxins in a new way for the purification of the receptor molecules. The *Naja* α-toxin was used as an affinity chromatography material, by attaching the toxin to an insoluble 'Sepharose' matrix. This material was then used successfully to separate the receptor molecules from acetylcholinesterase in solubilized electroplax preparations. No doubt further purification will be reported.

Changeux *et al.* also point out that the total number of receptor sites determined in their studies in electroplax preparations correspond fairly closely to the number of "receptor proteolipid" molecules reported recently from the same preparations by De Robertis and his colleagues (La Torre *et al.*, *Proc. US Nat. Acad. Sci.*, **65**, 716; 1970; De Robertis *et al.*, *Mol. Pharmacol.*, **7**, 97; 1970). These workers have used a completely different method for extracting a proteolipid fraction which has cholinergic receptor sites, as judged by its ability to bind radioactively labelled hexamethonium at curare-sensitive sites.

This sudden flourishing of molecular pharmacology seems to show no signs of abatement; each month now brings some new instalment.

CHROMATIN

Histone History

from our Molecular Biology Correspondent

Most workers in the field would probably agree that the state of knowledge about chromatin structure is one of the disappointments of molecular biology. In spite of prodigious efforts, the amount of hard information is dispiritingly small, and inadequate and contradictory results, not to say artefacts, have over the years been left lying like banana skins in the literature. The fact is that the system has turned out to be much more refractory than might have been hoped, and such successes as there have been have largely devolved upon the structure and properties of isolated components, such as the histones, the chemistry of which has recently been considerably clarified. In particular, the number of components is now known to be much smaller than was at one time supposed, and some of them have been meticulously characterized and even sequenced.

A feature of several of the histones is evidently a compositional polarization, one end of the molecule being strongly basic, the other preponderantly hydrophobic. This pattern must be expected to govern the conformation of the chain as well as its interaction with DNA. Recently, for example, Bradbury and his colleagues (*Nature New Biology*, **233**, 265; 1971) examined the separated halves of histone F2b, which by good fortune can be obtained by chemical cleavage at the two methionine residues, lying close together in the middle of the chain. The histone, it must be understood, is no globular protein, but rather a flexible chain which will change its structure in response to ionic strength, *p*H or temperature. The amino-terminal half contains most of the basic residues, and remains (as judged by optical rotatory dispersion) a random coil irrespective of ionic strength, and only by 2 M sodium chloride does aggregation set in. The other half by contrast becomes progressively more α-helical as the ionic strength increases. Proton magnetic resonance spectra indicate where, in the sequences of both halves, partial conformational freezing occurs, and it is the two regions (one at either end of the chain) which remain mobile and unaffected by salt that, on the evidence of earlier work, preferentially stick to DNA. This is consistent with the view of the histone as a glue which draws parts of a DNA chain together.

A similar picture emerges from the observations of Fasman, Valenzuela and Adler (*Biochemistry*, **10**, 3795; 1971) on the lysine-rich F-1 histone. This again has a polarized sequence, and can be chemically broken at a tyrosine into fragments of 6,000 and 15,000, the second containing the bulk of the lysines and also the prolines. Now when basic polymers are added in high molar ratios to DNA, a striking, though improperly understood, phenomenon is often observed, involving the inversion and magnification of optical activity of the DNA. Such an effect is encompassed by intact F-1 histone, and by the basic C-terminal piece, but not by the N-terminal fragment, though this too binds to the DNA. With both fragments together, the effect is enhanced to a level greater than that produced by the intact chain. The inference is that the C-terminal end is the structurally important DNA-binding site, and that the N-terminal part serves a modifying or cross-linking function.

The self-association of histones has also been advanced as a clue in determining chromatin structure, and it is

Embryonal Antigens and Human Carcinomas

Over the past several years a great body of evidence has been accumulated, indicating that the cells of malignant tumours, and cells transformed by carcinogens *in vitro*, carry antigens which are not found in normal adult tissues but can be detected in embryonic tissue. Last year, for example, Stonehill and Bendich (*Nature*, **228**, 370; 1970), working with mice, reported detecting embryonal antigens in a wide variety of carcinomas of adult mice and now Klavins, Mesa-Tejada and Weiss, as they report in next week's *Nature New Biology*, claim that "immunologically definable embryonic cell components are universally present in human carcinomas".

Klavins *et al.* raised anti-human embryonic antibody by repeatedly immunizing a rabbit with Freund's adjuvant and a lyophilized extract made from a 6-7 week old human foetus from an ectopic pregnancy. The serum from the rabbit was first absorbed against extracts from normal, adult, human heart, lung, spleen, kidney and intestinal tissue and was then tested by the Ouchterlony double-diffusion technique against extracts from a variety of human carcinomas including lung, breast and colon carcinomas.

The antifoetal antiserum cross reacted with all six sorts of carcinoma extracts, with extracts of normal, adult, human skin but not with extracts from corresponding normal adult tissues. In short, human carcinomas, but not normal adult tissues apart from the skin, carry antigens which cross react with antifoetal antisera. As Klavins *et al.* point out, such cross reactions do not prove that the foetal and carcinoma cells carry chemically identical antigens; but the fact that extracts of tumours and embryonic tissues behave identically on 'Sephadex G-200', as well as cross reacting in the Ouchterlony test, strongly suggests chemical as well as immunochemical identity. The mechanism by which embryonic antigens are caused to reappear after transformation to malignancy, and the exploitation of this phenomenon in diagnosis and perhaps therapy of cancer, will no doubt receive the attention they deserve.

known that some histones aggregate extensively in dilute salt solutions. Diggle and Peacocke (*FEBS Lett.*, **18**, 138; 1971) have shown, by osmometry and sedimentation equilibrium, that one species (F2c) does not aggregate at all, that three others (F2b, F2a2 and F3) aggregated in varying degree, and that F2a1 forms very large and apparently monodisperse aggregates. The results are in good accord, where comparison is possible, with inferences from PMR spectra.

In the altogether murkier area of whole chromatin, Itzhaki (*Biochem. J.*, **125**, 221; 1971) has drawn some conclusions from deoxyribonuclease digestion experiments. With two different nucleases, a considerable part of the DNA is hydrolysed, and appreciable amounts of protein, it is reported, are released with the soluble nucleotide material. The interpretation is that, since proteins fall off during the digestion, no very large tracts of DNA are completely bare. At some points these results are at odds with the findings of Clark and Felsenfeld, who found less (50 per cent as against 75 per cent) digestible DNA, without release of proteins. The displacement or migration of proteins is a hazard in this approach.

Clark and Felsenfeld accordingly performed their digestions under conditions in which they showed that the protein binding was not labile, and also when protein had been covalently attached to the DNA by prior chemical treatment. The reasons for the discrepancy are not therefore obvious. It may turn out to hinge on differences in the preparations, and on the properties of the urea-containing solvent used by Itzhaki, which, it is supposed, solubilizes free protein but not DNA-protein complexes. An interesting feature of Itzhaki's results is that in the presence of moderate magnesium concentrations chromatin is more rapidly digested than free DNA.

Just how careful one has to be in interpreting any results based on the interaction of enzymes with chromatin is the message that emerges from a paper by Hoare and Johns (*Biochim. Biophys. Acta*, **247**, 108; 1971). They measure the template activity of complexes of DNA with each of the main histone fractions as a function of the ratio of DNA to histone. Each fraction progressively inhibits the activity, and does so in a manner almost precisely paralleling the fractional precipitation of DNA. Because the same workers also showed that when the complex is solubilized by a large excess of histone (which moves it away from the charge equivalence region), the template activity is regained, it seems that this activity is substantially determined by the physical state of the material. The histone is evidently not capable in itself of blocking access to the polymerase.

NEONATES

Jaundice and the Pill

from a Correspondent

THE introduction of oral contraceptives in Britain in 1960 followed three years later by reports of breast milk as a cause of jaundice in young babies may be more than just coincidental. Oestriol—a derivative of oestrogen—when given to newborn babies is known to increase the level of bilirubin in the blood, making the infant jaundiced, and it has been suspected from *in vitro* studies that pregnanediol—a breakdown product of progesterone—is a factor which prevents the excretion of bilirubin (in fact, it inhibits the enzyme glucuronyl transferase which conjugates the bilirubin, making it water soluble and easily excreted by the kidneys). Almost all oral contraceptives are, of course, a combination of oestrogen and progesterone. But these hormones in the pill had not been considered as a factor in causing jaundice in babies because of the interval between the mother ceasing to take the pill and the birth of her baby.

It seems, however, from an article by Y. K. Wong and B. S. B. Wood of Birmingham Maternity Hospital, that the contraceptive pill and jaundice in the newborn may in fact be linked (*Brit. Med. J.*, **4**, 403; 1971). They report a prospective study of infants in the first few days of life who developed jaundice that was not attributable to any of the well-documented causes such as rhesus factor or prematurity.

Gaseous Diffusion in Homologous Series

REGULAR behaviour or systematic change in an observable property as a homologous series is traversed is always a welcome feature of an investigation, not merely because a regularity which is closely adhered to is a flattering reflexion of a carefully conducted set of experiments, but also because such a trend, particularly when linear, may sometimes be used for making predictions.

It is not really surprising to discover that the diffusion coefficients for the gaseous transport of a range of members of a homologous series through a common gas depend on the carbon number of the diffusing molecule. Some dependence would be expected, even on the basis of elementary diffusion theory, because the transport rate is a function of molecular velocity which is a function of molecular mass. What is surprising is that the dependence reported by Elliott and Watts in next week's *Nature Physical Science* is of such a simple linear form, namely

$$D = A\mu + B$$

where D is the diffusion coefficient of a member of the series into a common gas and μ is the reduced mass defined by

$$\mu = M_H\ M_G/(M_H + M_G)$$

M_H and M_G being the molecular weights of the homologous series gas and the common gas respectively.

Elliott and Watts have observed this relationship for the diffusion into air of a series of normal alkanes (paper presented at the twenty-seventh annual fall scientific meeting, Midland Section, American Chemical Society, October 24, 1970, and to be published in the *Canadian Journal of Chemistry*), but point out that results published in 1963 by Seager, Geertson and Giddings (*J. Chem. Eng. Data*, **8**, 168; 1963) also conform. In their latest communication Elliott and Watts only present results for the experiments of Seager *et al.*, but these, and also apparently those of Elliott and Watts, show that plots of D against μ are accurately linear (D decreasing with increasing μ) and that the intercept on the μ axis is close to the molecular weight of the common gas (for example, intercept 4.087 to 4.103 for He as common gas).

The predictive uses of this sort of simple linear relationship, particularly if it proves to be generally applicable to many different homologous series, are obvious. It seems likely that the applicability will be general because the series in the two systems described—normal alkanes (in air) and normal alkyl alcohols (in helium)—differ considerably in polarity. It is not clear, however, whether the relationship is still valid if the common gas has considerable polarity. Until the Elliott and Watts conference paper is published it is also not possible to decide to what extent the trend is primarily a mass effect and to what extent molecular shape and size play a part; this point could be checked by examining the diffusion coefficients of isomers of particular members of a series.

The theoretical interpretations of these observations are not clear, although the treatment of diffusion in binary systems in terms of realistic models is far from settled. The use of the reduced molecular weight is common practice when discussing diffusion in binary systems, but many of the published treatments (see Jost, *Diffusion in Solids, Liquid and Gases*, Academic Press; 1952) relate the diffusion coefficient to the reciprocal of the square root of μ; collision diameter is, of course, also an important factor in all existing treatments. It will be interesting to see to what extent Elliott and Watts have attempted to explain their observations in terms of existing models.

In an investigation of 116 mothers and their breast-fed infants, there was no correlation between jaundice and birth weight, gestation, sex, birth rank or age of mother. But, as Wong and Wood say, "Of the 69 non-jaundiced infants 24 (34.8%) mothers had been on the pill; of the 47 jaundiced infants 33 (70.2%) mothers had been on the pill." Fifty-seven mothers in the study had been on the pill and 59 had not. There seemed to be no difference in the pattern of pill-taking between those mothers who had taken the pill and whose babies were jaundiced, and those mothers who had taken the pill but whose babies were not jaundiced.

But Wong and Wood seem to be at a loss to account for the link between the increased incidence of jaundice and the pill; pregnanediol, for example, is always present in breast milk, but it is hard to see how its effect could be enhanced by the consumption of the contraceptive pill many months before breast feeding begins. Nevertheless, as Wong and Wood say, the figures speak for themselves, and will attract much attention among obstetricians and paediatricians.

FISH

Surgeon Fish's Scalpels

from our Marine Vertebrate Correspondent

SURGEON fishes are widely distributed herbivorous fishes of shallow tropical seas. Many species are known of these mostly colourful fishes and all possess a basic deep-bodied but laterally compressed form. Their common name is derived from a sharp scalpel-like spine placed either side of the body just in front of the tail fin; the spines resemble the surgeon's scalpel in both shape and acuity. These spines (members of four of the recognized genera have one each side; others have two or more) are attached posteriorly with the free sharp point projecting forwards, although the whole spine slots neatly into a groove in the side.

It seems axiomatic that fishes possessing such formidable armament should be able to use it in everyday life, and this aspect of the biology of the surgeon fish has recently been commented on by R. Winterbottom (*Copeia*, No. 3, 562; 1971). Winterbottom reviews earlier studies on the musculature of the spines. Although the presence of four superficial muscles attaching to the base of the spine had been described originally, later workers have been unable either to detect them or to prove an attachment to the spine. Dissection shows that apart from some connective tissue between the spine base and the superficial musculature the only important connexion is ligamentary between the spine and the posterior vertebrae. How then does the surgeon fish erect its spines for use?

Having studied the behaviour of living specimens in an aquarium when presented with a mirror, Winterbottom found that a strong response was evoked in the fish, which changed colour and raised its fins. More significantly, the fish would swim in a tight circle lashing its tail strongly as it passed the mirror. It also rested close to the mirror with body flexed and beat at its image with its tail. Winterbottom concludes from this and from handling the living fish that the spines are not muscularly controlled, but that they are partially erected by the bending of the tail as the body flexes. Thus when swimming strongly to escape, or in attacks on an intruder, the spines would be alternately exposed with each beat of the tail, and contact with them while the fish was moving forward would cause the erection of the whole spine into its fully exposed position as well as driving it into the adversary.

Several cases of wounds caused by surgeon fish in man have been recorded, some of them to persons carelessly handling live fish which presumably wagged their tails in escape movements driving their spines into their captor's hand. Several surgeon fishes appear to have envenomed spines and wounds from these species can be extremely painful. Even lacking an erecting musculature it is obvious that the surgeon fish's spines are more than adequate defensive weapons.

PHOTOCHEMISTRY

Nonlinear Photolysis

from our Molecular Physics Correspondent

AN important, though not unexpected, advance in photochemistry has been taken with the demonstration of what appears to be the first clear-cut two-photon decomposition reaction in the gas phase. S. Speiser, I. Oref, T. Goldstein and S. Kimel of Technicon, Israel Institute of Technology, now seem to have proved beyond reasonable doubt that the photolysis of azoethane ($C_2H_5NNC_2H_5$) observed when it is irradiated at very high intensity at a wavelength to which it is nominally "transparent" can only be due to the simultaneous absorption of two quanta of the available light (*Chem. Phys. Lett.*, **11**, 117 ; 1971).

The normal, well-studied photolysis of azoethane takes place with light at a wavelength of around 352 nm with a quantum yield of some 0.8. Speiser and coworkers selected the convenient ruby laser frequency of 694.3 nm and by means of a Q-switching arrangement were able to administer a series of pulses of extremely high energy in this region where normally nothing would be expected to occur. They duly observed the liberation of nitrogen and were able to show that its production was very nearly proportional to the square of the pulse intensity, indicating

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A Direct Acting Colicin

THE way in which that most curious class of proteins, the colicins, which are specified by extrachromosomal genes, are able to kill susceptible *E. coli* cells but do not kill their own host cells has long puzzled bacteriologists. In *Nature New Biology* next week, Nomura's group, adding another chapter to their most elegant exposition of the biology of colicin E3, explain how host cells develop specific immunity to this colicin and report evidence which suggests that the colicin penetrates susceptible cells and itself attacks their ribosomes.

Colicin E3 is, as Nomura and his colleagues and others have shown, a protein which kills *E. coli* by inactivating their 30S ribosomal subunits. The colicin causes a fragment of about 50 bases long to be cleaved from the 3′ end of the 16S RNA in the 30S ribosomal subunits. Until recently, most researchers who have worked with E3 and other colicins, which kill cells in quite unrelated ways, have suggested that these proteins remain on the surface of the cells to which they adsorb and mediate their lethal effect by causing some membrane change, rather than by entering the cell. This hypothesis now seems untenable as far as colicin E3 is concerned. Bowman, Sidikaro and Nomura have proved beyond doubt that *in vitro*, in the complete absence of any membrane, pure colicin E3 protein cleaves the 3′ end of 16S RNA in 30S ribosomes at the same point at which the 16S RNA is cleaved *in vivo*. In other words, the colicin attacks its target, the 30S ribosome, directly *in vitro*.

And that is not all. Bowman *et al.* have discovered that cells which carry the colicin E3 genetic factor and make E3 protein contain a substance or substances which protect the colicinogenic cell's ribosomes from attack by the colicin. In other words, cells which make colicin E3 are able to survive because they make an antagonist to E3. Presumably, past failures to detect *in vitro* the activity of colicin E3 reflect the fact that the impure preparations of colicin used contained this protective substance(s).

The fact that colicin E3 can act directly *in vitro* strongly suggests that *in vivo* it penetrates susceptible cells and directly attacks their ribosomes, rather than causing some change in the cell surface which in turn inactivates the ribosomes. If this is true of colicin E3, then it may well be true of other colicins.

that photolysis was occurring with the absorption of two quanta, as though at an effective wavelength of 347 nm. The two-photon reaction cross-section proved to be $6.5\pm2.5\times10^{-52}$ cm^4 s/photon mole, probably the first measurement of its kind.

Two-photon effects have been demonstrated before in solution reactions (for example, see S. Speiser and S. Kimel, *J. Chem. Phys.*, **51**, 5614; 1969), although in these the unpleasant complication of solvent effects is worsened by the strange phenomenon of self-focusing in the laser beam. This occurs when the light intensity becomes so great as to modify the refractive index of the liquid and cause a lens-like focusing towards the beam axis. Although this, if anything, increases the tendency to two-photon reaction, it complicates considerably the calculation of effective cross-sections, because the true intensity profile must be estimated through the nonlinear optics involved.

Although a satisfactory theory of multi-photon rate processes may be some time in arriving, it is perhaps not too soon to ponder some of the problems which are raised by the existence of such processes. The first will not worry anyone unduly, although it is amusing: where ultra-high intensities are involved one must now exercise some caution in referring to a substance as "transparent" to a certain wavelength so long as an absorption band is present higher up the energy-scale. Second, and more serious, it is perhaps time to ask whether quite new photochemical influences may be at work under these conditions where the magnitudes of electric and magnetic field vectors in the neighbourhood of the molecules become so enormous. Any peculiarities which may emerge as the theory of dielectrics at extreme fields develops may well prove to have chemical effects not simply connected to the transition probabilities for photon absorption.

ZOOLOGY

New NERC Unit

THE Insect Pathology Unit (under Dr T. W. Tinsley) at the University of Oxford, which has been supported for the past five years by a grant in aid from the Natural Environment Research Council, has now been brought directly under the council with the title of Unit of Invertebrate Virology and with Dr Tinsley as director. The unit will carry out basic studies on the viruses and viral diseases of invertebrates.

PLANT ENZYMES

Coordinate Induction?

from our Phytochemistry Correspondent

SUBSTRATE induction of enzymes (that is, their synthesis in response to the presence of their substrates) is now commonplace in microorganisms and not infrequent in higher animals. In higher plants, however, substrate induction is a rare phenomenon and it is therefore gratifying to see significant progress being made towards the full understanding of the one well authenticated example, the induction by nitrate of the nitrate assimilation system. The latest advance in this campaign is the demonstration by Kelker and Filner (*Biochim. Biophys. Acta*, **252**, 69; 1971) that nitrate induces both nitrate and nitrite reductase in a simultaneous rather than a sequential manner. It has been known for several years that the application of nitrate to plants previously grown on nitrate-free medium led in many cases to the appearance of high levels of nitrate reductase and nitrite reductase, the enzymes which catalyse the first two reactions in the reductive assimilation of nitrate. In 1966 Ingle, Joy and Hageman (*Biochem. J.*, **100**, 577; 1966) reported a three-hour lag between the induction of nitrate reductase and that of nitrite reductase in radish cotyledons and proposed that the rise in nitrite reductase activity was dependent on the prior formation of nitrite by the action of newly formed nitrate reductase. In other reports, however, identical time-courses for the appearance of the two enzymes in response to nitrate were found, supporting a simultaneous rather than a sequential induction mechanism.

To test this question critically, use was made of the knowledge that tungstate inhibits the development of nitrate reductase (a molybdo-protein), probably by being incorporated in place of molybdenum, thus forming a non-functional enzyme (Wray and Filner, *Biochem. J.*, **119**, 715; 1970). Using exponentially growing tobacco cells in suspension culture, Kelker and Filner showed that transference from a nitrate-free medium to a medium containing both nitrate and tungstate led to normal appearance of nitrite reductase in the absence of any increase in nitrate reductase activity. In these conditions, added nitrate could not be converted *in vivo* into nitrite and the authors logically conclude that nitrate directly induces nitrite reductase. Earlier this year, the same group provided evidence that nitrate induces the formation of the nitrate-uptake system in tobacco cells (Heimer and Filner, *Biochim. Biophys. Acta*, **230**, 362; 1971) while in barley shoots nitrate also induces an NADH-cytochrome *c* reductase (Wray and Filner, *ibid.*).

It seems clear, therefore, that the development of several biochemical activities intimately involved in the

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Genes to Switch off Host

WHEN bacteriophages such as P22, λ, or the T even phages infect bacteria the overall RNA and protein synthesis of the infected cell is either transiently or permanently depressed. Where a lysogenic phage such as P22 is involved this depression of the host's macromolecular metabolism is permanent if the infection leads to cell lysis, but transient if it leads to lysogeny. The possible role of phage genes in these changes has been widely debated for many years and in next Wednesday's *Nature New Biology* Chakravorty and Bhattacharya of the Banaras Hindu University report experiments which clearly implicate genes of phage P22 in the inhibition of RNA and protein synthesis in *Salmonella typhimurium*.

Exploiting mutant as well as wild type phage, Chakravorty and Bhattacharya established that the extent of inhibition of RNA and protein synthesis depends on the multiplicity of infection and also that RNA and protein synthesis can be independently depressed. They then measured the depression of macromolecular synthesis when *S. typhimurium* cells, lysogenized either by wild type P22, which has an intact *sie*$^+$ gene and specifies an active sie protein, or by mutant *sie*$^-$ phage, are superinfected with wild type P22. The RNA and protein synthesis of lysogens carrying the mutated *sie*$^-$ gene is transiently depressed on superinfection. By contrast, superinfection with P22 does not depress the metabolism of *sie*$^+$ lysogens. In other words, cells which carry a *sie*$^+$ gene and make active sie protein—which may well be analogous to the *C* gene repressor protein of phage λ—do not suffer transient depression of their macromolecular synthesis on superinfection, because the sie$^+$ protein prevents expression of any of the genes of the superinfecting phages, including those which somehow interfere with host metabolism. Experiments with a mutant of P22, which is virulent probably because it does not respond to the *sie* gene repressor, support this argument. Superinfection of a *sie*$^+$ lysogen with the virulent mutant P22 results in a transient depression of RNA synthesis.

In summary then, the depression of cellular RNA and protein synthesis following infection with P22 appears to depend on the expression of some P22 genes, which is probably regulated by the product of the *sie* gene.

assimilation of nitrate by higher plants is regulated by nitrate in a manner which, at least superficially, resembles the coordinate regulation of the *lac* operon in *E. coli*. Although it would be dangerous to conclude from this that similar mechanisms are at work in *E. coli* and tobacco cells, it is nevertheless cause for some celebration whenever the plant kingdom is brought one step nearer the molecular empire. It is to be hoped that further probing of the nitrate assimilation system will lead to discoveries of importance for our understanding of the regulation of gene expression, not only in plants, but also in other eukaryotes.

REVERSE TRANSCRIPTASE

Enzyme with Many Uses

from our Cell Biology Correspondent

A SUPPLY of radioactively labelled DNA molecules complementary to either messenger RNAs or the genomic RNAs of the RNA viruses is something molecular hybridizers have long dreamed of; as specific probes, such DNA molecules would be invaluable when it comes to detecting, for example, the location of genes on chromosomes, the sites of replication of RNA viruses or specific RNAs or DNAs in complex mixtures. The discovery of reverse transcriptase raised hopes that such DNAs might become available; everything depended on the degree to which this enzyme in RNA tumour virus particles is template specific. If reverse transcriptase shared the rigid template specificity shown by phage Qβ RNA replicase—an enzyme which can only use Qβ RNA and variant molecules derived from it—its use would be very restricted, but what if tumour virus reverse transcriptase proved to lack substantial template specificity? This enzyme could then be used to make a DNA complementary to all sorts of RNAs. In the event, as Spiegelman, Watson and Kacian report (*Proc. US Nat. Acad. Sci.*, **68**, 2843 ; 1971), the reverse transcriptase isolatable from avian myeloblastosis virus particles (AMV is readily available in large quantities, unlike many other RNA tumour viruses) seems to lack rigorous template specificity.

This enzyme, which when pure has been shown to consist of equimolar amounts of two polypeptide chains weighing 110,000 and 69,000 daltons (Kacian *et al.*, *Biochim. Biophys. Acta*, **246**, 365 ; 1971), will reverse transcribe, albeit at different efficiencies, not only AMV RNA and synthetic homopolymer duplexes but also natural RNAs from sources as diverse as Qβ phage and Moloney mouse sarcoma virus. In short, reverse transcriptase lacking template specificity should prove to be an enormously useful enzyme.

And if the experiments of Crippa and Tocchini-Valentini (*Proc. US Nat. Acad. Sci.*, **68**, 2769; 1971) and Ficq and Brachet (*ibid.*, 2774) are anything to judge by, it seems that an RNA dependent DNA polymerase (reverse transcriptase) may exist in eukaryotes and play a crucial part in processes such as gene amplification. During oogenesis in the toad *Xenopus laevis* genes specifying ribosomal RNA, which, including a spacer DNA, form a unit about 9×10^6 daltons, are amplified. Crippa and Tocchini-Valentini have attempted to implicate a reverse transcriptase in this process. They have shown, using 5-bromodeoxyuridine as a density label, that the ribosomal DNA cistrons are not themselves apparently used as a template for their own amplification. This finding suggests, of course, that the template for the amplification of the ribosomal DNA cistrons may be an RNA rather than a DNA.

Crippa and Tocchini-Valentini have also shown that, albeit at fairly high concentrations, 2′,5′-dimethyl-N(4′)benzyl-N(4′)[desmethyl]rifampicin, a drug which is known to inhibit the activity of reverse transcriptase in tumour viruses (Gurgo *et al.*, *Nature New Biology*, **229**, 111 ; 1971), inhibits gene amplification during oogenesis in *Xenopus*. This, of course, suggests that the enzyme responsible for amplifying these genes may be a reverse transcriptase. Ficq and Brachet, using autoradiography to monitor the amplification of ribosomal DNA in *Xenopus* oocytes, also show that this drug inhibits the process and draw the same conclusion. It may well be therefore that ribosomal DNA amplification depends on the transcription of the ribosomal DNA cistron into a 47S RNA transcript which is then used as a template by reverse transcriptase.

Laser Studies of Vibrational Energy States

THE availability of high-powered monochromatic beams of laser light, which are well collimated and usually polarized, together with the fact that they may be modulated or pulsed in times as short as 10^{-11} s, has promoted research into many new areas in the field of electromagnetic/vibrational energy interaction.

Energy distribution among the various vibrational modes of single molecules and the interchange of vibrational energy between molecules following laser excitation have become fruitful areas of investigation in recent years. Selection of a laser wavelength which exactly matches an absorption line in a molecule makes it possible to populate efficiently a single vibrational energy state. At present more than twenty vibrational bands, exactly matched by laser frequencies, are known. The rates of the various vibrational energy transfer processes which follow the absorption may be determined with comparative ease and this fact, together with the rapidly expanding number of systems which are becoming amenable to experiment, has made both practical and theoretical approaches profitable.

Since the simultaneous appearance in the literature of the first two reports of laser excited vibrational (infrared) fluorescence, the first involving the asymmetric stretching mode (001) of carbon dioxide and the second involving the bending mode of methane, laser excited vibrational fluorescence experiments have considerably increased the detailed understanding in this field. Several kinds of chemical lasers have been described. Typically, infrared fluorescence originates from rotational lines in the vibrational spectrum of HCl which is formed by flash photolysis of fast flowing mixtures of chlorine and hydrogen. In HCl–CO_2 mixtures both HCl and CO_2 fluorescence have been observed.

In the closely related techniques of double resonance which may involve infrared, microwave or a combination of both kinds of radiation, changes in the vibrational–rotational energy distribution produced by the absorption of a pulse are monitored by means of absorption changes. In the presence of strong monochromatic resonant radiation molecules no longer assume a Boltzmann distribution. If the radiation is applied continuously a steady state will be produced in which the population of a particular level n_i is different from that for a Boltzmann distribution n_i°. The value of $n_i-n_i^\circ$ depends on the power of the radiation and the relaxation time between the levels. Double resonance techniques enable the values of $(n_i-n_i^\circ)-(n_i-n_i^\circ)$ to be measured and therefore provide a powerful insight into the mechanisms of relaxation processes. Collisional relaxation of the (100) state of CO_2 itself has been studied by this technique using CO_2 lasers as pumping and monitoring sources while the more general applicability of the method has been demonstrated in a study of the relaxation processes in SF_6.

As well as the energy transfer studies already mentioned, some uncertainty about the initial absorption process still remains, particularly in cases where the high photon density of the laser beam brings about the involvement of multiquantum processes. In particular, the communication by R. T. Bailey, F. R. Cruickshank and T. R. Jones in next Monday's *Nature Physical Science* should help to resolve some problems.

SURVEY OF NORTH AMERICAN SCIENCE

Signs of Change in Science Policy

In the past few months, Washington's science policy machinery has been working overtime on plans that could significantly alter relationships between science and government in the United States. The result of all this work is likely to be a change of direction in American science policy rather than a wholesale increase in the total research and development budget, and although industrial technology will probably be the chief beneficiary, the universities are also likely to feel some eddies from the winds of change that are swirling around the White House.

What is going on in the scientific bureaucracy is no less than an attempt to redirect and stimulate research and development along lines that will help to solve economic and social problems—in essence another form of the white-hot technological revolution hailed by Mr Harold Wilson as the answer to Britain's economic problems in the early 1960s. Four chief factors have combined to stimulate the Administration's interest in science and technology: unemployment, which among scientists and engineers is running at its highest level since the war, the flagging domestic economy, the trade deficit and the especially bad trading figures for high technology products. But perhaps the chief factor in the drive to find new ways to put science and technology to better social use is the desire to inject new life into the economy and reduce the numbers of unemployed in time for next year's Presidential election.

The ideas that are now being discussed in the White House will, however, have an impact that is likely to outlast any temporary pre-election boom, for they call for a rather fundamental change in the relationship between government and industry on all kinds of research and development. In short, what is happening is that some members of the White House staff are busily engaged in sifting through a list of scientific projects submitted by industry and by government agencies, and it is hoped that a package will be put together in time for next year's budget message so that President Nixon can announce that the Administration is backing a range of socially-orientated technological projects. The backing is likely to take the form of tax incentives or even subsidies which will make the government a partner in all kinds of industrial research. Another part of the package may be a relaxation in the anti-trust laws to allow companies in the United States to get together on research and development in areas such as pollution control.

Such ideas are not new—they have been canvassed in various government departments for years—but until recently there has been little serious attempt to take a firm grip on the problems involved in making a reality out of the political rhetoric that says that science and technology should be brought to bear on social problems. In the heady days of the 1950s and early 1960s, the vague promise that a brave new world would be built from science and technology was sufficient to justify pouring more and more dollars into science's coffers. Before long, however, administrators began to look more closely at the relationship between research and economic growth, and the budgetary emphasis was placed on those technologies likely to have some payoff for national well-being. The latest moves in the Administration are effectively aimed at first determining the problems and then looking around not only for new technologies that may help to solve them but also for ways to adapt old technologies in new ways.

The Office of Science and Technology began almost a year ago to look around for such new "technological initiatives", but the project did not really begin to take on a definite shape until this summer, when two senior members of the Administration—Maurice Stans, Secretary of Commerce, and Murray L. Weidenbaum, Assistant Secretary of the Treasury—hinted in testimony to a Congressional committee that something strange was afoot in the upper echelons of the science bureaucracy. Stans suggested that some method should be found for stimulating civilian research and development because the level of investment in this sector during the past few years has been stagnant. The upshot, he suggested, has been that the United States is sitting on the sidelines watching other countries grow and prosper and that it is about time that serious consideration was given to such devices as loan guarantees, cost sharing, grants and procurement incentives for stimulating industrial research and development. Weidenbaum maintained that "there are strong indications that as a nation we may now become too niggardly in our overall support of science, engineering and the related intellectual activities that are so fundamental to our growth and progress". His chief suggestion was that the government should consider tinkering with the tax structure to provide some incentive for firms to offset the risks involved in embarking on technological projects.

In September, all these various trains of thought were brought one step nearer realization when William M. Magruder, the Administration's champion of the ill-fated SST, was appointed to the White House staff with the title of special consultant to the President on links between research and development and high technology exports. His appointment, made without fanfare, caused barely a ripple in the White House watcher corps, until it became obvious that his brief is much wider than his title suggests. He is, in short, the man who has been charged with the task of coordinating and expanding the "technology initiatives" project started by the Office of Science and Technology, and with stimulating civilian research and development.

Magruder's appointment is widely viewed, at least out-

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side immediate White House circles, as a slap in the face for the Office of Science and Technology, for he has effectively taken over the chief responsibility for one of the OST's most important programmes; there has been no shortage of speculation that his appointment marks a downward shift in the influence of Edward E. David Jr., the President's Science Adviser and head of the OST.

The OST staff in fact reacted to the appointment with some misgivings, but they are now saying that Magruder is more an ally than a threat to their influence, because the OST is in any case not properly equipped for dealing with such a highly political issue. David himself says that Magruder's appointment has not affected the status of the OST, and that his own relations with the President have not been changed at all. There is no denying, however, that the "technological initiatives" programme is an important area of policy in which the OST has already invested considerable time. Indeed, the outcome of the project is likely to determine many facets of the Administration's links with science, and therefore the relegation of David to a secondary role does not augur well for the OST or for the influence of academic scientists.

What effect the Administration's newfound interest in research and development is likely to have on the overall scientific effort is open to question, but there seem at present to be few prospects of a bonanza for basic research in the budget that is now being put together in the White House. The way that budgetary restrictions have already bitten into academic research in the United States can be seen in several institutions like the Princeton-Pennsylvania accelerator which is limping along on private funds because the Atomic Energy Commission's budget could not accommodate it along with the increased funding for the National Accelerator Laboratory at Batavia. In many respects, the decision to deprive the Princeton-Penn accelerator of federal money is symbolic of the fact that the halcyon days of academic research, in which money was made available for all types of project on the slightest justification, are finally at an end.

In 1968, total government expenditure on research and development started on a decline that was only halted in the Administration's budget for the present financial year. Even the 7.6 per cent increase in expenditure asked for in that budget was, however, insufficient to offset the inflation over the past few years, and there were still warning signs that scientists must justify their requests for federal money as rigorously as any other group. To be sure, much of the decline in the science budget could be put down to a slackening in the space programme as the Apollo series nears its end, but the very real signs of financial stringency in the universities bear witness to the fact that budgetary restrictions are biting deep.

The state of high energy physics, apart from the financial situation of the Princeton accelerator, is a good example of how funding policies have changed. The problem here is that the National Accelerator Laboratory is soaking up an increasing share of the funding for higher energy physics, and other enterprises are being cut out as a result. In the not too distant past, the total high energy physics budget might have grown to accommodate the increasing cost of the National Accelerator Laboratory, but the weaker laboratories now have their backs firmly to the wall. The Joint Committee on Atomic Energy, in its report on the authorizations for the Atomic Energy Commission this year, in fact warned that the trend of declining high energy physics funds must be sharply reversed if all existing laboratories are to be kept open, and asked the AEC for a priority listing of which establishments should be kept open if budgets continue to decline.

Radio astronomy is yet another area where insufficient funding has caused undue belt tightening. Three years ago a panel under the direction of Professor R. H. Dicke of Princeton University drew up a list of projects on which the Federal government could usefully make a start but, so far, the only suggestion taken up is that a new surface should be provided for the Arecibo telescope. Another review of the standing of astronomy has, however, just been completed by a panel under the direction of Professor Jesse Greenstein of California Institute of Technology, and it seems that radio astronomy may get a long overdue injection of funds in the coming budget.

Another field of research that can face the future with confidence—at least as far as funding is concerned—is cancer research in particular and health research in general. The tussle over the organization of cancer research that has occupied two congressional committees and many lobbyists on Capitol Hill during the past year has been remarkable not so much for the ideas that have been put forward, but for the fact that it has been almost taken for granted that, however cancer research is finally administered, it will enjoy a massive budget. The Administration's stake in the enterprise has already been demonstrated by President Nixon's request for an extra $100 million for cancer research this year, and by unceasing efforts of the White House to get its name on whatever legislation finally goes through Congress.

The Administration's preoccupation with applied research is also likely to leave its mark on the budget for the National Science Foundation, at least as far as the portion devoted to the programme known as Research Applied to National Needs (RANN) is concerned. This year's budget for the NSF in fact represents an increase of some 22 per cent compared with the money the foundation spent last year, the chief increase being for funds devoted to picking up projects shed by other agencies, such as the materials research laboratories transferred by ARPA. But the budget that finally emerged from the Congressional mill was very different in character from that requested by the Administration.

Congress, in short, applied the knife to some of the projects that the Administration had wanted to stimulate, such as RANN, and added funds to some of the educational programmes, such as institutional and graduate support, that the Administration had wanted to run down. The upshot was that Congress gave the Administration the $622 million it asked for, but the Office of Management and Budget immediately impounded $32 million of the extra money voted for educational support as part of "the anti-inflation plan" thereby reducing the foundation's total budget to some $590 million.

The rationale behind the desire to cut out some of the funding for graduate support is that the pool of unemployed scientists and technologists is already embarassingly large, and the Administration wants to slow down the rate of production of postgraduates. The whole tug of war is, however, likely to have a second showing next year if the Administration continues on the same tack—and to judge by its recent fascination with applied research and with reducing the numbers of unemployed, a repeat performance is certainly possible.

ASTRONOMY

Twenty-five Years of Rocket and Satellite Astronomy

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On October 10, 1946, a V-2 rocket, instrumented by the Naval Research Laboratory, was launched from White Sands, New Mexico, and carried an ultraviolet spectrograph above the ozone layer to photograph the solar ultraviolet spectrum. After twenty-five years of rocket astronomy, it is therefore appropriate to trace some of the history of astronomy from space platforms.

SUPPORT for space research in astronomy in the United States has been generous and on the whole the scientific returns have been very rewarding. The flow of new information is in the mainstream of the remarkable progress of present day astronomy and promises to influence our understanding of the universe even more profoundly in the future.

The V-2 flight in 1946 enabled R. Tousey and his NRL colleagues to photograph the solar spectrum down to 2200 Å. Similar success quickly followed from the efforts of J. J. Hopfield and H. E. Clearman, jun., of the Applied Physics Laboratory. From these beginnings rocket astronomy moved on to a remarkable series of advances in solar spectroscopy, which eventually mapped the entire spectrum to its X-ray limit and led naturally into the study of celestial objects beyond the solar system. Of great importance to all this solar research was the biaxial pointing control developed at the University of Colorado with support from the Air Force Cambridge Research Laboratory.

Photometer Developments

While the first photographic spectrographs were being flown, my colleagues and I sought to develop narrow band photometers for the ultraviolet and X-ray portions of the spectrum. A set of photon counters sensitive to X-rays (1–8 Å) and the ultraviolet bands 1050 to 1350 Å and 1425 to 1600 Å were flown in 1949. This flight provided quantitative measurements of solar X-rays, the hydrogen Lyman-α line and the Schumann continuum region of the ultraviolet; it also gave a comprehensive picture of solar–terrestrial relationships in the D, E and F-regions of the ionosphere. Encouraged by the success of this simple photometric technique we moved on to the exploration of a wider range of astronomical sources.

The earliest attempt (1955) to measure stellar ultraviolet emission employed wide field of view photon counters on an Aerobee rocket. Above 85 km the Lyman-α sensitive detectors quickly saturated in the intense resonance radiation of the hydrogen geocorona. First, by narrowing the field of view and then by moving on to telescopic mirror collection systems, it was possible to do far ultraviolet photometry of early-type stars. In a typical Aerobee rocket flight (utilizing the free spin and precession to scan the sky) the fluxes of some 200 stars could be measured in several ultraviolet bands. When the NASA astronomy programme was conceived at the beginning of the last decade, the early rocket results afforded guidance in planning the series of Orbiting Astronomical Observatories (OAO).

Rocket Fuels

Liquid-fueled rockets were satisfactory for preassigned launch schedules to observe the X-ray and ultraviolet emissions of the quiet Sun but could not be kept in the launching tower in a "hold" status to await a transient event such as a solar flare. To explore the flare phenomenon, the NRL group made use of the Rockoon, a combination of the Deacon solid propellant rocket and Skyhook balloon. From the deck of a Naval vessel in the Pacific a Rockoon was floated at 80,000 foot each day for ten consecutive days during the summer of 1956 while we waited for evidence of a flare. When a flare occurred, the rocket was ignited by radio command and climbed above the 100 km level to observe the flare radiation. Clear evidence was obtained of the production of hard X-rays by a solar flare and the penetration of this radiation to the base of D-region (about 60 km).

This exploratory effort was followed by the use of two-stage solid-fueled rockets in the International Geophysical Year (IGY) and the accumulation of evidence of flare X-rays of energy up to 100 keV. The rocket experiments led eventually to the Navy Solrad programme which in 1961 began to monitor solar X-ray variability and which is continuing with Solrad-10, launched in July 1970. For refined spectral detail astronomers have used the NASA Orbiting Solar Observatory programme, which recently placed OSO-7 in orbit. This series has provided high resolution X-ray and ultraviolet spectra, as well as ultraviolet spectroheliograms and X-ray images, and the OSO programme is planned to continue through this decade.

An early clue to the possibility of galactic and extragalactic X-ray astronomy came out of the Rockoon Solar Flare Program in 1956. A scintillation counter covering the energy region 30 to 200 keV showed a background flux that was separable from atmospheric emissions. Aerobees flown in the years from 1957 to 1962 carried detectors which searched unsuccessfully for celestial X-rays but the breakthrough finally came with the discovery by Giacconi, Paolini, Gursky and Rossi in 1962 of X-ray emission from the general direction of the galactic centre. Since that historic date X-ray astronomy has produced a succession of surprising discoveries following one on the other in rapid succession.

Advent of Satellites

At the beginning of the 1960s space research in the United States moved into the satellite era. Rocket astronomy had mapped the full solar spectrum to wavelengths as short as a few Å, recorded the transient X-ray bursts of solar flares, photographed the Sun in Lyman-α and in X-rays, discovered the geocorona and measured the far ultraviolet fluxes of early-type stars. These pioneering observations stimulated the planning of the first generation of astronomical satellites but the value of continuing with rockets, and to a lesser extent balloons, as platforms for space astronomy was clearly established.

Throughout the 1960s rocket astronomy continued to lead the way to new discoveries in the ultraviolet and X-ray regions, and the basic ideas for future orbiting astronomical observatories were shaped on the basis of these discoveries. X-ray and gamma ray astronomy, in particular, have generated such interest that the chief astronomy effort in the NASA programme for this decade will be the High Energy Astronomical Observatory series (HEAO).

Some fifty discrete X-ray sources have been found within the galaxy and perhaps the greatest interest centres on those which exhibit various forms of extreme variability. Although the catalogue of radio pulsars has grown steadily, the list of X-ray pulsars includes only the Crab pulsar with certainty. Bursts of pulsar-like emission have been observed from Cyg XR-1, but their lifetimes seem to be transient. Several periodicities from 73 ms to 290 ms have been reported at different times with flux variations as great as a factor of ten. It is difficult to fit this complex behaviour to existing theoretical models of rotating objects. Only in auroral X-ray phenomena have similar transient pulsation characteristics been observed. Cen X-3 shows no radio pulsation but is almost fully modulated in X-ray emission at a period of about 5 s and exhibits abrupt increases and decreases of a few hundredths of 1 per cent in period during time intervals as short as a minute. Is it a neutron star or a white dwarf near rotational instability? Tentative evidence has recently been obtained by Sadeh from an NRL balloon flight of X-rays from NP 0527 at a period of about 4 s. If true, X-rays are emitted from the fastest and slowest radio pulsars, which presents quite a dilemma for existing theories. Furthermore the X-ray period is 2 per cent longer than the radio period. Could this be a relativity effect?

The list of extragalactic X-ray sources now includes the Magellanic clouds, the quasar 3C 273, Seyfert galaxies NGC 1275 and NGC 4151, the Virgo and Coma clusters, the jet galaxy M-87 and the more typical radio galaxy, Cen A. In each of the peculiar galaxies the X-ray source provides the principal portion of the total radiated power. X-ray astronomy of these objects should provide important clues to the mechanisms of nuclear activity. Where several observations have accumulated in recent years, as for M-87, evidence exists for large flux and spectral variations on a time scale as short as a few months. Is the variable emission associated with a spinning super-massive object ($>10^6\ M_\odot$), groups of magnetoids of $10^4\ M_\odot$ in the jet or swarms of millions of pulsar-like objects? Is the intense infrared emission from NGC 1275 directly coupled to the X-ray emission, does the X-ray emission heat a dust shell to produce infrared emission, or does the X-ray flux derive from Compton scattering of relativistic electrons on synchrotron infrared quanta in a compact core of diameter about one light year? More refined spectral data and frequent monitoring from satellites will help to answer these questions.

Diffuse Background

Many rocket and satellite observations have confirmed the existence of a diffuse X-ray background which is highly isotropic above 10 keV. The most restrictive limits on spatial fluctuations were derived from OSO-III data in the 8 to 38 keV range by Schwartz and Peterson. Since the discovery of the diffuse background, there has been speculation about whether the source is the sum of unresolved galaxies or whether it arises throughout intergalactic space.

From the high degree of X-ray isotropy, Wolf and Burbidge have argued that super-clusters of galaxies (about 10^6 galaxies over a region of about 50 Mpc) can be ruled out. If the background is produced by high energy electrons within galaxies, or if it leaks out into the surrounding intergalactic space, a map of the X-ray background should resemble the distribution of galaxies. There is no evidence of such anisotropy in the background X-rays and the observations would therefore seem to exclude super-clusters or the still greater hierarchy of super-super-clusters as the source of X-ray background. It is, in effect, possible to deny on the basis of isotropy the production of background radiation from the sum total of galaxies unless we resort to evolutionary models in which most of the X-rays come from early epochs when the distribution of galaxies may have been much more homogeneous.

For several years, rocket astronomers in the United States, Canada and Japan have sought to extend the X-ray background spectrum to energies as low as 100 eV. As the results become more refined and reliable, it becomes clear that the spectrum bends upwards below 1 keV. Whether this excess is local or extragalactic is still a controversial question; one interpretation is that the soft X-rays are bremsstrahlung radiation from intergalactic gas at $\sim 10^6$ K and that the density accounts for 97 per cent of the mass of a closed universe.

Clusters of Galaxies

During the past year rocket and satellite observations have been made of the large and distant clusters of galaxies in Coma and Virgo. Each cluster contains thousands of galaxies which presumably radiate X-rays like the Milky Way. NRL rocket observations revealed X-ray fluxes about twenty times as great as would be expected from the individual galaxies, and it was suggested that this excess is produced by hot gas ($T > 8 \times 10^6$ K) within the clusters. More refined measurements of Coma by the UHURU satellite showed the emission to be concentrated near the centre of the cluster. The mass of gas would not exceed about $6 \times 10^{13}\ M_\odot$, or about 3 per cent of the total mass of the cluster, which is insufficient to bind the cluster gravitationally. Therefore, unless the cluster contains a large amount of mass in the form of neutron stars and black holes, its component galaxies should be dispersing.

Gott and Gunn have argued that infall of intergalactic gas ought to fill the cluster to a much higher concentration over a period of 10^9 yr than the limit set by the X-ray observations, if the intergalactic gas density is about 10^{-5} cm^{-3}—the critical value for a closed universe. In effect, the accumulation of no more than $6 \times 10^{13}\ M_\odot$ implies a limit on the intergalactic gaseous medium of less than 10 per cent of the mass of a closed universe, according to their estimates. Thus the first-generation measurements of X-ray background and galactic clusters have raised as many questions as they have answered but any models of closed or open universes, of bound or unbound galaxy clusters, must now confront a great deal of new observational evidence.

Future Space Research

A recent study of priorities for space research by the National Academy of Sciences gave greatest weight among new starts in astronomy to HEAO, and recommended a programme of four launches in this decade. The giant spacecraft will weigh 21,000 pound and will be 30 foot long by 8 foot in diameter; its payload of scientific instruments will weigh about 12,500 pound. High energy astronomy can exploit such large payloads to great advantage in cost effectiveness over rockets or the SAS-class satellites. Whereas SAS-1 could accommodate about 2 foot^2 of X-ray proportional counter sensitive to a narrow band from about 2 keV to 7 keV, the X-ray survey instrument for HEAO-A will have an area of about 60 foot^2; it will cover the wide range from 0.2 keV to 200 keV and will have far greater data handling capacity. The individual millisecond pulses of the Crab pulsar, for example, will be recordable with high signal-to-noise ratio. Yet this instrument will cost less than twice that in SAS-1 and will be only one of seven instruments of comparably advanced power for X-ray, gamma-ray, and cosmic-ray observations included in the total payload of the first HEAO scheduled for 1975.

A vigorous rocket and balloon programme during this decade is not made any the less desirable by HEAO. Balloon astronomy is highly effective for studying variability and 1,000 pound payloads can routinely be raised to 150,000 foot for

10 h of observation. Considerably improved instruments are being developed for rocket astronomy and rockets with an order of magnitude greater payload weight and volume could be made available from military surplus at low cost. The NAS study referred to previously recommended a doubling of rocket and balloon support for astronomy, even at the lowest contemplated budget level.

Trends in Optical Astronomy

As the natural follow-on to the OAO programme, the astronomical community supports the goal of a major optical astronomy facility in space, the large space telescope (LST), for the 1980s. It would have an important impact on cosmology. Today's ground-based telescopes cannot establish the value of the deceleration parameter with sufficient certainty to distinguish between an open and a closed universe. At the very best, it may be possible to measure redshifts and to measure galaxies photometrically to magnitudes 21 to 23 with the largest ground-based telescopes. An LST would help greatly to solve the problems of the size and structure of the universe. With better than 0.1 arc sec resolution (3 m mirror) a limiting magnitude of ~ 29 for stellar photometry is attainable, about a hundred times fainter than the ground-based limit. This capability should indicate the cosmological scale and curvature of the universe and provide a great deal of information on the evolution of galaxies at different epochs.

The orbiting of an LST would be such a large undertaking that its useful lifetime must be counted in decades. If the Space Shuttle should become available in the 1980s the desired maintenance capability would be assured. In this decade we may look to the launching of a half-scale prototype (1.5 m diameter) as a step toward the eventual LST.

Although European space astronomy seems to have abandoned plans for a large optical telescope in the near future, much emphasis is being placed on high energy astronomy. UK-5, a 270 pound spin stabilized X-ray astronomy satellite to be launched in 1973, will have improved capabilities over SAS-1. The European Space Research Organization (ESRO) has under consideration a lunar occultation satellite with a 200,000 mile apogee. Its X-ray detector will aim a 3° field of view at the Moon and thus observe a large number of source occultations with second of arc precision. Plans for small X-ray astronomy satellites are also going forward in Japan and the Netherlands; Soviet Cosmos satellites have carried X- and gamma-ray detectors as has Lunakhod-1. Undoubtedly such programmes will be further developed in the decade.

The first quarter century of astronomy from space platforms has brought us to a new generation of very advanced spacecraft and payloads and substantial opportunities for more effective use of rockets and balloons. From the modest vision of the small band of scientists who formed the V-2 Atmospheric Research Panel in 1946, we have come to the imminent realities of "Palomars" in space and the prospects of probing deeply into the universe in every wavelength of the spectrum.

CANADA

Science Policy and Canadian Manufacturing Industries

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This article examines the factors which determine the amount of research and development undertaken in Canadian industry and suggests that the influence of multinational corporations must be carefully incorporated into future science policy.

"MAJOR emphasis must be placed on the importance of using science and technology in support of the nation's social and economic goals". In its fourth report, *Towards a National Science Policy for Canada*, the Science Council of Canada in 1968 thus directed its attention along a path which brought its interests closer and closer to the topics of current debate. The council's work in the past three years has focused on the application of science and technology to such important problem areas as urban development, the natural environment, transportation, resource use and computerized communications. Most recently, the council has been primarily concerned with the problems of innovation in Canadian industry. Rather than attempt to review all the problems of today's Canadian science policy debate, I shall concentrate on the set of interrelated issues that dominate our concern about Canada's industrial science and technology. These are (i) the lack of traditional employment opportunities for highly qualified manpower[1]; (ii) the cessation of growth and now the decline of industrial research and development activity in Canada[1]; (iii) the difficulties of Canada's high-technology manufacturing industries[2], particularly following the imposition of the United States import surcharges in August; (iv) the pervasive influence of the chiefly USA-owned foreign corporations which dominate the high technology sector of Canadian industry[3].

The work done so far has failed to uncover any sound economic theory which could indicate whether or not there is some fixed minimum proportion of a country's economic activity which should be devoted to manufacturing. Perhaps such a minimum does not exist and policies in Canada should be geared entirely to the resource and service sectors of the economy; but nothing convincing has been written to shake the intrinsic faith in the idea that there should be at least some manufacturing activity, preferably in the higher technology areas, to provide stimulus and challenge to our increasingly well educated labour force. It is the sign of weakness in this activity which prompts the current concern.

Employment Prospects

Canada continues to have an unusually high annual growth in her labour force. It was 2.5 per cent a year during the past decade, for example, compared with 1.5 per cent in the United States, 0.4 per cent in Britain; the even more rapid increase in the proportion of highly qualified scientists and engineers in the labour force has been particularly marked during the 1960s. Following the 1961 census which exposed Canada's considerable dependence on immigration as a source of trained people, it has been explicit government policy, at both federal and provincial levels, to expand university facilities, enrolments and opportunities for postgraduate research. The success of this policy is now evident; in 1970 Canada's per capita output of PhDs in science and engineering finally exceeded that of the United States. The problem of the supply of highly qualified people in many fields has been successfully overcome, so much so that a new problem has now emerged because Canada has failed to generate a high enough demand for such people, particularly in the traditional employment areas of research and development, and has failed to identify new ways to make use of them.

Demand for Manpower

The late 1960s and early 1970s have seen the three traditional sources of employment in the field of research and development dry up simultaneously. Hiring by government departments and agencies was cut back to a mere trickle following the government's decision in 1969 to impose austerity budgeting as part of its fight against inflation. The rate of expansion of university staffs, which has been about 13 per cent throughout the 1960s, was abruptly moderated and is now about 5 per cent, so the universities are absorbing a significantly reduced fraction of their own output. This leaves the industrial research and development sector which will be the principal focal point of this article.

In 1968 and 1969 Canada's industrial research and development activity reached a peak (at an expenditure level of about $410 million) and has, in real terms, slowly declined since then[1]. As so much attention has in the past been devoted to research and development in Canadian industry, this decline must be seen as a serious setback for existing policies. Of 36,000 industrial corporations in Canada only 640 have any research and development activity at all and more than 500 of these have ten or fewer professional (that is, graduate) employees engaged in this type of work. It is revealing to note that the 1970 output of science and engineering PhDs in Canada exceeded the entire stock of PhDs working in industrial research and development in the country.

Concern that Canada has been "doing too little research and development in industry" has been rife since the OECD started publishing comparative statistics on research and development in member countries in about 1963. Not only did Canada's gross expenditure seem too low (about 1.4 per cent of GNP) but the fact that industry accounted for only about one-third of it was taken to indicate a significant structural problem in need of a remedy.

Canada's federal government adopted an approach to remedy the situation which was unique in the Western world, when it enacted a series of "incentive programs"; these have been evolved over several years and the principal ones at present are the Program for the Advancement of Industrial Technology (1965) and the Industrial Research and Development Incentives Act (1967). These programmes relegated government to a passive role of provider of some assistance to research and development programmes devised by industry, in the form of grants or forgivable loans—forgivable, that is, if the project failed. Other countries have tended to cast government in the more active role of purchaser of research to meet goals designated by government. In retrospect, the Canadian incentives had some unforeseen flaws—they were tied to short term increments of growth of research and development activities and no support was given to the stabilization of existing activities; they also failed to consider the provision of a market for any successful innovation, a market which government purchasing power might have assured. When economic circumstances worsened, industrial research and development failed to command a share of many corporate budgets.

Manufacturing Industries

The Science Council of Canada recently published a report[2] which attributed the current malaise in Canadian manufacturing to a series of problems. These were principally: (*a*) the inadequacy of the technological base of most companies; (*b*) the fragmentation of the domestic market for many products and the existence of barriers which inhibit entry into export areas; (*c*) the inadequacies of the management of many Canadian enterprises; (*d*) the poor climate for investment in Canada (reflected in the excessive caution of Canadian investors); (*e*) the improper location of some industries. The first three of these problems are aggravated by the dominating presence of foreign owned corporations in Canada's economy.

Table 1 Foreign Ownership, Foreign Control and Research and Development Performance Distributions in Canadian Manufacturing Industry

	Foreign ownership (%)	Foreign control (%)	Distribution of industrial expenditures on research and development (%)
Electrical	70	78	29.1
Chemical	66	80	23.6
Transportation	82	80	17.8
Metals	51	51	9.8
Machinery	62	54	4.2
Pulp and paper	53	48	4.5
Utilities	18	4	11.0
Miscellaneous	50	59	

This topic is discussed at length in ref. 3.

Foreign Ownership

To encourage the growth of employment opportunities Canada has traditionally offered tariff protection to resident industries and has encouraged direct foreign investment throughout the economy. The net effect of these twin policies has been the emergence of an unusually high proportion of foreign owned and controlled industries in Canada, particularly in those sectors where most Canadian industrial research and development is performed (Table 1).

The traditional conclusions drawn from such data have usually stressed that foreign corporations have been doing more than their fair share of research and development in Canada. Further study of the situation has indicated that such a conclusion is simplistic, and that a case can be made that Canada is suffering from the unforeseen and adverse effects of a surfeit of "technology transfer" which previously had been regarded as an unmixed blessing. The most important manifestation in Canada of foreign ownership is the extensive presence of subsidiaries of large multinational corporations and it is through these enterprises that technology transfer most frequently occurs.

The success of the multinational corporation is often ascribed to its ability to manage technology. Having invested large sums of money in the development of a new product or process, it is in the interest of the corporation to maximize its returns on this investment by transferring the new technology into production in as many locations as possible. The "higher" the technology, the bigger the investment needed and hence the greater the incentive to establish production subsidiaries abroad, behind tariff walls. This logic may well lie at the root of the large concentration of foreign ownership in Canada's high technology manufacturing sector.

The typical Canadian branch plant subsidiary possesses little "technological depth"; it is not set up in a manner which permits it to innovate but rather it receives most of its technology from its parent—production drawings, materials specifications and even specialized parts flow into the Canadian operation from abroad. As an example of this lack of depth, at least one of "Canada's" chief automobile manufacturers imports a team of engineers from the United States each year to carry out annual model change modifications to its production line. Under such conditions there is little scope for individual management initiative and the spirit of the entrepreneur is stifled.

The advantage of technology transfer to the branch plant is a substantial reduction in the overhead charges associated with the generation of new technology, which in turn allows the subsidiary to exist while having only a small share of the Canadian market—a share which would be too small to support a domestic corporation which depended on generating its own technology. Although a subsidiary may exist under such conditions and although its internal economics might make it appear globally competitive, it will often not have a mandate to seek export markets in which it might compete with the parent or a related subsidiary, so the opportunity to expand based on international trading is denied. In effect the subsidiary trades the option of exporting in return for transferred technology.

For such branch plant subsidiaries, their dependence on technology imported from a foreign parent has meant that they offer: (i) little or no employment of highly qualified people, especially in research and development, because there is no mandate to innovate; (ii) little or no opportunity for the development of aggressive management and entrepreneurial skills; (iii) a ceiling on overall employment imposed by the limitations of the demands of the Canadian market (21 million people); and (iv) substantial impediments to a domestic corporation breaking into the already badly fragmented Canadian market because the domestic corporation would have higher overheads associated with the development of its own technology.

Not all subsidiary operations are branch plants, however, and it is important to place in context the research and development efforts of the multinational corporations which operate in Canada. These efforts can broadly be classified as being one of two dominant types: (*a*) a small facility whose chief preoccupation is the scaling down of imported technology to suit Canadian tests, conditions and smaller markets, or (*b*) a highly specialized laboratory which may have no connexion with the production activities of the same company in Canada; any successful innovations emerging from such a "rationalized" research and development operation could lead to production in the parent country, the host country or some third country depending on which location would optimize the returns to the whole operation. In such a case a Canadian incentive grant for research and development could well be a subsidy for the creation of manufacturing jobs and profits in some other country. The whole operation creates a rather special kind of "brain drain" in which the individuals do not leave the country but their ideas do.

Strategies for Canada

The outcome of studies by the Science Council on industrial research and development has been a preliminary delineation of the many influences of foreign ownership and multinational business which pose constraints on Canada's ability to take initiatives in the industrial sector. These problems are today perceived as political issues; they are widely debated and much studied, and a ministerial task force at the federal level has been investigating the implications of foreign ownership for Canada. Although different parts of the political spectrum may regard the existence of multinational corporations in our economy from widely differing points of view, all must recognize that these corporations are now an economic fact of life, that their influence on world trade may well grow and that each host country must find ways of ensuring that subsidiaries make an adequate contribution to the realization of the goals of the host rather than only to those of the parent or third nation. Control of the multinational corporation is difficult for both host countries and those countries in which their headquarters are located. The administration in the United States claims, for example, that United States investment overseas is equivalent to "exporting jobs". To control their own multinational corporations the United States administration has backed a Bill, now before Congress, proposing the establishment of a "Domestic Industrial Sales Corporation" designed to offer tax incentives to corporations which "repatriate" manufacturing jobs.

For Canada, more than any other Western country, the need to learn how to live with the multinational corporation and to have it contribute to the country's goals is urgent. Experience has shown that the approach of the research and development incentive programmes has assumed that promotion of research would be a panacea, the source of improved productivity and ultimately of increased industrial activity and more jobs. This approach has not been successful and a new one is needed.

The Science Council of Canada has been strongly underlining Canada's need for a clearly articulated industrial strategy. Although the problems raised in this article need solution, they are not the only ones facing the would-be strategist and any final policy will be found only in the broader context of the nation's concern about the costs and benefits of industrialization, about employment, education and environment and about the fostering of social justice in the world today.

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[1] Kelly, F. J., *Prospects for Scientists and Engineers in Canada*, Special Study No. 20 (Science Council of Canada, April 1971).

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GEOPHYSICS

Alive and Well

from our Geophysics Correspondent

This article describes both the state of geophysics research in the United States and some of the directions in which it is moving.

It is quite impossible to give anything like a balanced account of the state of geophysics in the United States in the space of a short article. All one can really do is declare it to be alive and well and point out some of the salient features, begging the pardon of those who are not mentioned. The American Geophysical Union has a membership of more than ten thousand and geophysics as a discipline covers everything from cosmic rays to seismology by way of planetology, hydrology, meteorology, volcanology, oceanography, tectonophysics and geomagnetism. So this article will describe a limited sample of geophysical activities, based on a personal predilection for the solid Earth.

Sources of Finance

Geophysics could not have reached its present healthy state without a large infusion of money and it is therefore worth looking briefly at the sources. The diversity of these sources is the strength of the science. One single national organization devoted to distributing research funds—the system that most countries have adopted—has many merits but the American system is a valid counter-example. If you have no luck with your grant application at the National Science Foundation you can always try the National Academy, the Advanced Research Projects Agency (ARPA), the Air Force, the Army, the Navy, the Atomic Energy Commission, the oil companies, the National Ocean Survey, NASA, several foundations and one or two favourably disposed millionaires. In recent years the environment movement has been given a perhaps undeserved boost by the establishment of geophysics departments in many smaller universities aiming to "cover" the environment with three or four diverse professors. Perhaps it is here that geophysics is showing signs of over-reaching itself. Some of those lured with promises of shining new departments are expressing disillusion at the expense of maintaining an adequate geophysics programme and the waning of university enthusiasm when it comes to fitting out laboratories and acquiring data; this at a time when the traditionally large earth science schools such as Columbia, Harvard, MIT, Berkeley, Caltech and San Diego are being themselves confronted with a decline in available funds. ARPA's project VELA, for example, which injected $150 million into geophysics in the 1960s for nuclear test detection is now a rapidly shrinking programme. NASA is a doubtful quantity. The 1970 Mansfield amendment restrained military spending in universities. As yet the belt-tightening has not cut very deep, and good undergraduates continue to flow into the subject. A PhD in geophysics is still more in demand than a PhD in physics but the signs of levelling out are everywhere.

American geophysicists confine themselves to the continental United States no more than do American soldiers. This is perhaps most clearly seen in the marine sciences. Lamont, Woods Hole and Scripps, the traditional seagoers, have been joined by a score or more of other oceanographic institutes with their own deep-sea vessels. Most of these have identified some particular region as their own parish and few have opted for the nearest offshore region. Magnetic, gravity, heat-flow and air gun surveys are widely undertaken and magnetics, of course, has been the most profitable with its huge returns in the field of seafloor spreading. The JOIDES drilling programme has been a brilliant success in inter-university co-operation, and perhaps will lead to a more national approach to some of the geophysics projects (such as ocean bottom instrumentation) which are too complex for individual groups. Palaeomagnetism of cores is vigorously pursued and dredging seems to be losing its association with black magic. Seismic refraction, conversely, seems to be in decline, perhaps because of its expense and the frequent ambivalence of its results.

Availability of Data

The thing that strikes the visitor to any American geophysical laboratory is the sheer volume of data. This has made the American research worker much more able to capitalize on discoveries than his counterparts elsewhere. Perhaps this was most strikingly seen when plate tectonics burst onto the scene. Laboratories which had accumulated large amounts of magnetic data and which had access to the global data of the World-Wide Seismic Network were able to move in rapidly and, within a year or two, to have the subject remarkably well documented. Lamont–Doherty's extraordinary vigour in this direction is worthy of special note.

At the present D. Karig's ideas on the structure within island arcs is attracting much attention and, one suspects, papers are being written which give strong support to the concepts. Also J. Morgan's hotspot hypothesis is being followed with interest but it suffers from a lack of crucial experiments which has as yet prevented its wholehearted acceptance. This bashfulness does not seem to extend to graduate students who, with customary enthusiasm, are explaining the world's remaining problems in terms of behind-arc-spreading and hotspots. One hopes that they are right. Apart from the hotspot hypothesis, causes of continental drift as opposed to its consequences are apparently receiving scant attention. This probably stems from the large amount of work required to determine stress fields in the mantle by comparison with the smaller amount necessary to explain the observed features of a small section of the globe by plate tectonics.

Seismology, traditionally the largest branch of geophysics, is at present in transition. The VELA programme is drawing to a close and the emphasis is shifting; with detection, location and identification as its prime concern, it was a shot in the arm for classical seismology and caused research on the mantle and the core to become an integral part of solving the problem. Now an excellent data base has been developed from individual stations, arrays and new generation instruments and classical seismology is well supplied for several years to come. The new topics of interest seem to be high pressure geology, the nature of earthquakes, their prediction and control. As seismologists have been making finer distinctions in their models of the mantle, it has become a question of growing interest whether certain deep boundaries that seem to exist fairly consistently throughout the world can be associated with changes in mantle composition under high pressure and temperature. A cognate and even more interesting question is whether, if the precise depth of these discontinuities is known, laboratory studies on "rocks" of different composition can indicate which composition is the most likely. O. L. Anderson of UCLA and D. L. Anderson of Caltech have played an important role in following up the early work of F. Birch of Harvard and several laboratories are now extensively committed.

Using Teleseismic Data

An equally flourishing programme on earthquake sources is in progress. There was a time when seismology could do little with teleseismic data from earthquakes except use them to determine Earth structure but the work of L. Sykes (Lamont) on reliable focal mechanisms changed the picture immensely. Now J. Brune (San Diego), K. Aki (MIT) and their students are providing a clearer picture of the fundamental parameters of an earthquake—size of fault plane, moment, stress, stress drop and rupture velocity. This is being done by a combination of teleseismic observations and "near-in" instrumentation for Californian earthquakes. This looks a very promising field, and one with almost unlimited scope because of the many different types of earthquake.

Many Americans were, of course, at the International Union of Geodesy and Geophysics in Moscow in August and one of the consistent impressions that they brought back was of the success that the Russians were having in earthquake prediction. Success in this context is not yet to be construed as more than an ability to forecast earthquake-prone regions as a function of time. The prediction programme in the United States has been centred on the San Andreas Fault, and the Earthquake Mechanisms Laboratory in San Francisco and the Geological Survey in Menlo Park have been prime movers. An impressive amount of instrumentation is now deployed along the fault for the study of micro-earthquakes and premonitory tilts and strains. Progress is being made but there are still some problems in store. This was made clear by the San Fernando earthquake of last February, an event which gave no premonitory signs and which occurred on a fault which few had even heard of. The speed with which geophysicists got to work on documenting the San Fernando quake was impressive; within a day, local networks had been established to study aftershocks and, within two months, coherent accounts of the earthquake, its aftershocks and its effects were being presented.

As the physics of the earthquake source is pursued some startling new ideas are arising. The role of fluids in the vicinity of a fault is being increasingly appreciated as a result of both laboratory experiments and field observations. Tests are now being conducted in the Rangely (Colorado) oilfield by B. Raleigh and J. Healy of the Geological Survey which indicate that micro-earthquake activity is correlated with the fluid pressure in the fault zone. Pressures higher than hydrostatic pressure seem to unlock the fault in some way and to allow strain adjustments by means of earthquakes. The implications of these experiments for an earthquake control programme are obvious and it may not be long before geophysicists ask for a mandate to look at somewhat more significant fault regions.

Lunar Geophysics

The lunar geophysics programme throws out a healthy batch of problems. A lunar "crust" seems to be emerging from observations of well timed impacts of spacecraft on the Moon but the seismogram complexity is still far from resolved. The hour-long energy train recorded after impacts is generally attributed to a highly heterogeneous Moon full of scattering centres but the latest and most irreverent explanation is in terms of non-linear oscillations of the seismometer itself. Time, presumably, will tell. The discovery of periodicity in moonquakes is quite remarkable. Correlation with perigee is striking, and all the more surprising because years of research on earthquakes have failed to reveal a single correlation with extra-terrestrial sources.

One of the quieter evolutions in American geophysics seems now to have been completed. Gravity and magnetics have theorems which limit the amount of interpretation which can be applied to observations of potentials and in general geophysicists work within the confines of these restrictions. Seismologists had no simple theorem and, particularly in the interpretation of the Earth's density and elastic properties, models spawned in the mid-1960s. Now, however, some restraint can be applied. The work of G. Backus and F. Gilbert (San Diego) on inversion has set limits to what a finite data set with assumed standard deviations can reveal about the Earth. No simple two line explanation can be given of what the implications are—the papers have to be read. R. Parker, also of San Diego, has extended the Backus–Gilbert work into the domain of electromagnetic sounding where the need of it may be felt in the near future with a substantial increase in the deployment of magnetometers.

Geophysics, presumably, continues to survive in the prospecting industry which is understandably unwilling to brag about new technology. One suspects, however, that since the swing to digital recording and controlled energy sources with all the associated new concepts they brought the emphasis has been firmly on routine implementation of good techniques rather than on further research into new methods. No survey, however inadequate, of American geophysics should fail to mention the excellence of the services provided by the National Ocean Survey (formerly Coast and Geodetic Survey) which acts as a stable backdrop to the frantic activity of the academic geophysical community.

GENETICS

Genetic Analysis of Developmental Mechanisms in *Drosophila*

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The fruit fly *Drosophila* is being increasingly used in embryological experiments. Because of its well known genetics, and the ease with which the larvae can be manipulated in a variety of ways, it provides an ideal system for following such processes as cellular determination during differentiation, and cloning in morphogenesis.

When Thomas Hunt Morgan left embryology for genetics he deserted *Hydra*, planaria, sea urchins and amphibia for *Drosophila*. The fruit fly was recognized, and still is recognized, as an ideal organism for the study of eukaryote genetics, but it now seems that it will turn out to be equally suitable for answering many questions concerned with development. The fact that the *Drosophila* genome is midway in size and complexity between that of *E. coli* and that of mammals[1] makes this organism a logical choice for analysing the molecular biology of development, just as *E. coli* was a logical choice for analysing the molecular biology of heredity. The possibilities of *Drosophila* in the study of developmental biology were realized long ago by Stern, Hadorn, Poulson, Bodenstein and others. In recent years, however, interest has increased and we wish to review some recent trends in the analysis of its development.

Drosophila, like all holometabolous insects, lives what Snodgrass[2] has called a "double life"; that of the larva and that of the adult. After the completion of embryonic development (about 22 hours after fertilization) the resulting larva hatches and enters a growth phase lasting about four days. The larva then transforms to a pupa, and during the succeeding four days completes its metamorphosis to form the adult. During metamorphosis many of the larval tissues break down and most parts of the surface of the adult are constructed from small nests of cells in the larva, known as imaginal disks. There is a disk

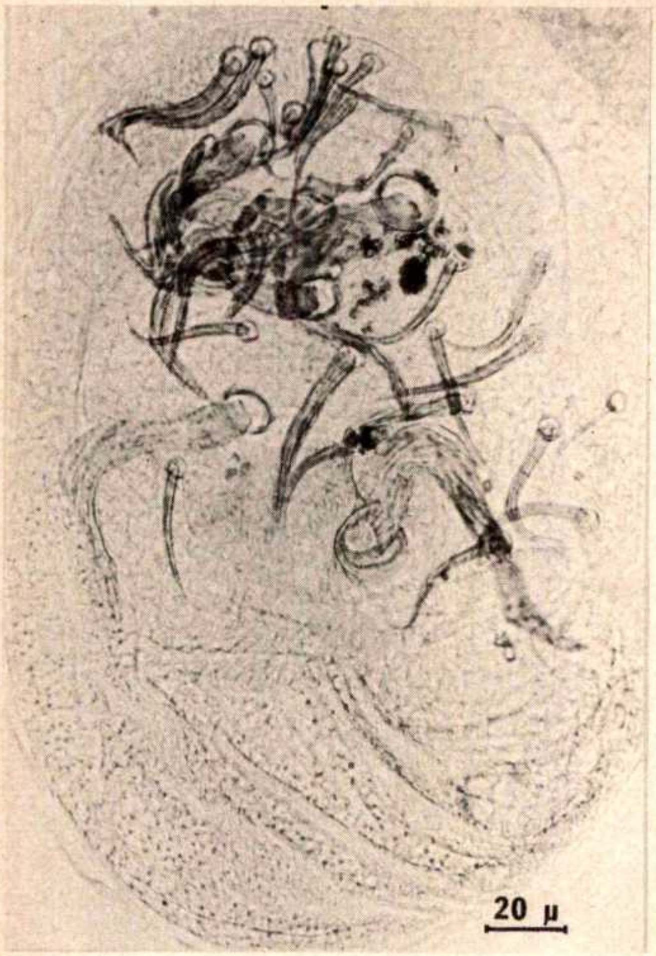

Fig. 1 Adult structures (thorax bristles; *yellow, singed*[3] genotype) derived from nuclear transplants into unfertilized eggs. From Schubiger and Schneiderman[14].

representing each adult leg, one for each wing, and so on. These imaginal disks are set aside early in embryonic life and never become a functional part of the larva. They grow in size as the larva grows but they remain undifferentiated; their cells resemble those of embryos. Much of the recent research has been concerned with these essentially embryonic tissues as well as with the embryo itself.

The Embryo

The eggs of insects do not undergo cleavage in the usual sense. In *Drosophila*[3], the cleavage nuclei undergo about eleven rapid divisions without separation of the cytoplasm into cells. About two hours after fertilization the nuclei enter the peripheral cytoplasm—the cortex—at a stage known as preblastoderm. At this time the nuclei probably begin to synthesize RNA[4]. Then they become separated by cell membranes to produce the cellular blastoderm embryo. This stage is shortly followed by gastrulation and the remainder of embryonic development. Most of the recent work on *Drosophila* embryology has been concerned with the early stages, and in particular with the question of when during development the cells or nuclei become determined to construct particular parts of the larva or adult. That is, when do their developmental capacities become firmly established ?

A strong impetus to these studies has come from the finding[5,6] that parts of embryos can be grown in the abdomens of adult flies. These parts complete embryogenesis in these conditions, and produce recognizable larval structures as well as tissues which will differentiate into adult structures when transplanted to host larvae for metamorphosis. This discovery greatly extends the possibilities for experimental embryology with *Drosophila*, because pieces of the embryo can be manipulated in various ways without the necessity of ensuring the survival of the whole embryo. Using this technique with the 10 h embryo, Schubiger *et al.*[7] were able to show that head structures and genitalia were formed only by cells from the anterior and posterior embryo halves, respectively. Hence, the different regions of the antero-posterior axis of the embryo had by that time become determined. More recently, Chan and Gehring[8] have applied this technique to the embryo at the blastoderm stage, and they have shown that the anterior and posterior halves of an embryo at this early stage are already determined for the anterior and posterior structures of the adult, respectively.

The evidence for determination at the blastoderm stage, coupled with evidence from other insects indicating that the cleavage nuclei are multipotent, has suggested to several workers that the basic pattern for the embryo may be established in the cortical cytoplasm even before the cleavage nuclei enter it[9]. The cells would then acquire their different determinations as the nuclei come to lie in diverse microenvironments within the cortex. It has been assumed that this is the case chiefly as a result of experiments indicating that a special region of the cortex of the egg, known as the pole plasm, influences the immigrating nuclei such that this region gives rise to the germ cells. Irradiation of this region of cytoplasm with an ultraviolet microbeam invariably produces sterile animals[10]. The idea that regions of the cortex other than the pole plasm exert analogous influences on the remainder of the nuclei has never been tested critically, however. Attempts to test this hypothesis have been made both by analysing the developmental consequences of defects made in the cortex of young embryos, and by transplanting nuclei and cytoplasm between embryos.

In the most recent defect experiments by Nöthiger and Strub (unpublished), accurately localized ultraviolet microbeams were used to produce burns in the cortex of embryos at early cleavage stages. Adults with various defects were obtained, but there was no correlation between the position of the burn and the position of the resulting defect in the adult. These findings are in contrast to those of Illmensee (cited in R. Nöthiger and S. Strub, unpublished), who found a topographical correlation between the positions of punctures made later in preblastoderm embryos and the positions of defects in the resulting adults. Hence, if the cortex is organized so as to exert localized determinative influences on the immigrating nuclei, it seems that this organization must develop at some time between the early cleavage and preblastoderm stages. During this brief period of about 2 h, the basic pattern of the adult organism seems to be mapped out.

The technical *tour de force* of insect surgery, nuclear transplantation in *Drosophila* eggs, has now been achieved in several laboratories. Geyer-Duszynska[11] and Illmensee[12] first reported limited development of unfertilized eggs after injection of nuclei from cleavage stage embryos. No adult structures were produced, however. Illmensee[13] and Schubiger and Schneiderman[14] have extended these experiments by culturing tissue from the defective embryos in adult abdomens. After transplanting this tissue to host larvae for metamorphosis, they were able to show that the transplanted nuclei had survived to eventually produce adult structures (Fig. 1). This was true whether the nuclei were injected into fertilized or unfertilized eggs. More recently, Zalokar[15] has finally succeeded in obtaining adult animals from fertilized eggs which had been injected with nuclei. Genetic markers were used to demonstrate the participation of the implanted nuclei in the development of both larval and adult structures.

These successes open up a new field of experimentation in *Drosophila* developmental genetics. The technique can be used to prove or disprove the idea of the multipotency of cleavage nuclei. Furthermore, it should be possible to identify the factors that might produce specific microenvironments in the cortical cytoplasm, by transplanting pieces of cortex

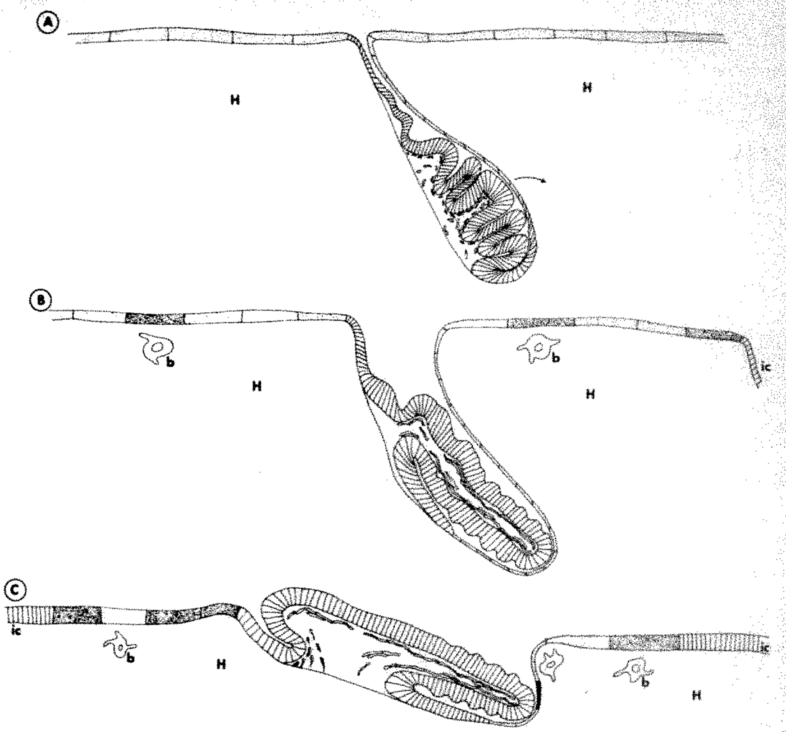

Fig. 2 Diagram to illustrate the process of eversion in a leg disk. *A*, The disk epithelium in the mature larva is a single layer of epidermal cells, continuous with the larval epidermis through the disk stalk. *B*, 3–5 h after initiation of metamorphosis, the disk is partially unfolded and partially uncovered. *C*, 5–6 h after initiation of metamorphosis, the developing leg is almost completely unfolded and uncovered. Imaginal disk cells (ic) sequentially replace the larval epidermal cells. H, Haemolymph; b, blood cell. From Poodry and Schneiderman[18].

between embryos and by implanting cytoplasm from differentiated cells into embryos. Further, one can begin analysing the processes of differentiation by means of the transplantation into eggs of nuclei from older stages.

Another approach to understanding the organization of the egg is through the study of mutants in which the homozygous female produces defective eggs. A particularly intriguing example is the mutant grandchildless of *Drosophila subobscura*[16]. The grandchildless females lay eggs whose pole plasm is abnormal, so that no germ cells are formed in the embryos, and the resulting adults are sterile. In *bicaudal* other parts of the egg are abnormal, so that embryos develop with two abdomens and no anterior parts[17]. Workers in several laboratories are searching for other mutants of this type, in the belief that studies of eggs with abnormal organization will provide clues to the mechanisms involved in normal development.

Imaginal Disks

The imaginal disks of *Drosophila* have recently attracted increased attention as model systems for the analysis of several developmental problems such as morphogenesis and pattern formation. As a basis for developmental and genetic studies several workers[18–20] have studied the morphology of these organs and the morphological changes occurring during their development. The encouraging part of their findings is the simplicity of organization of the imaginal disks. Poodry and Schneiderman[18] established that they are basically folded sacs consisting of a single-layered columnar epithelium. The disks also contain some nerve cells, and adepithelial cells which are probably muscle precursors. Their origin in development as invaginations from the embryonic epidermis is consistent with this type of organization, and their change in shape to that of the adult structure (the process of "eversion") can easily be understood in terms of an uncovering and unfolding of the epithelial sac (Fig. 2). The conversion of the tightly folded epithelium of the disk to the entended adult structure represents a spectacular morphogenetic movement. This is especially true of legs, where it has been shown that the change in shape of the cell sheet is related to a change in cell shape from columnar to squamous[18]. Certain changes also occur in the cell junctions, the most obvious being a great increase in the number of septate desmosomes. Brief treatment with trypsin causes the disk to undergo eversion *in vitro*, indicating that changes in intercellular adhesion, as well as changes in cell shape, may be important in causing the eversion movements[21].

One of the reasons for our interest in imaginal disks is that their development can be analysed by the use of genetic mosaicism. The technique which has been particularly useful is X-ray induced somatic crossing over[22]. With this technique single cells in the imaginal disks can be made homozygous for recessive marker genes (for example, *yellow*, *singed*) while the cells in the rest of the animal are heterozygous (Fig. 3). All the progeny of the affected cells are also homozygous for the marker gene (or genes), so the resulting clones are recognizable as coherent patches of mutant tissue on the surface of the adult. Thus X-ray induced somatic crossing over permits the investigator to follow the developmental activities of the descendants of a single cell with great precision.

One striking result from these studies is that, in many parts of the adult, clones are markedly non-random in shape. The clearest case is that of the leg (Fig. 4) in which clonally related cells form long narrow strips of tissue often extending over several leg segments[23]. Some clones have been found to be over 100 cells long without exceeding a few cells wide. This indicates that there is a predominantly radial alignment of daughter cells in the developing disk, which may be one of the important factors determining its structure. Similar longitudinal clonal patterns are present in wing disks[24,25].

Some scattered reports in the literature reveal that such clonal patterns are not unique to *Drosophila*[26]. Spontaneous mosaics in wasps and bees show longitudinal stripes in the legs, and in wasps and moths similar patterns are found on mosaic wings. This leads us to conclude that oriented cell division may be a common feature of developing insect appendages. Furthermore, the fact that most clones are continuous and with smooth outlines persuades us that there is little individual cell movement in these systems.

Data from somatic crossing over experiments can be conveniently used to measure various parameters of imaginal disk development. Clone size in the adult depends on the stage of irradiation, because the number of cell divisions which are to occur before metamorphosis decreases with larval age. Hence the average clone size following irradiation at various stages can be used to estimate the cell numbers and rates of cell division in the disks at these stages. We have shown, for example, that the leg disk begins its developmental career as a

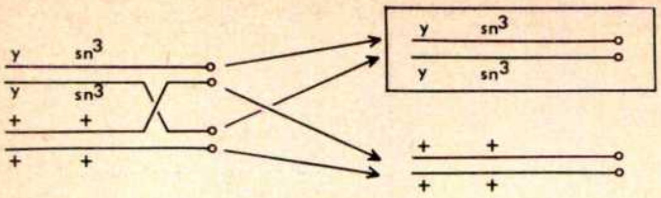

Fig. 3 Diagram to illustrate the process of somatic crossing over. Recombination between two chromatids from homologous chromosomes leads to homozygosity of the daughter cells. The $y\ sn^3/y\ sn^3$ daughter cell (boxed) produces a clone of cells with $y\ sn^3$ phenotype, distinguishable from the rest of the animal which has a wild type phenotype.

group of about twenty cells in the embryo, and that it grows throughout larval life with an average cell cycle time of about 15 h, until the time of metamorphosis[23]. The wing disk grows somewhat faster, with an average doubling time of about 11 h[24]. The abdominal tergites represent an unusual situation, since the anlagen for these structures do not appear to increase in cell number during larval life, but do show rapid growth during the initial stages of metamorphosis (M. Guerra, J. H. Postlethwait and H. A. Schneiderman, unpublished, and personal communication from J. Merriam and A. Garcia-Bellido).

In the antennal disk, studies of the cell lineage pattern by Postlethwait and Schneiderman[26] have disclosed that its development is basically similar to that of the leg disk, but with the addition of several twists and bends late in development. The correspondence in developmental processes in the leg and antenna has also been illuminated by studies of the homoeotic mutant *antennapedia*, in which the antennae are transformed into various grades of leg-antennal intermediates[27]. Detailed analysis of these intermediates revealed that each location on the antenna corresponds exactly to an equivalent location on the leg, as indicated by the occurrence of characteristic bristles, sensilla groups, and other position-specific structures (Fig. 5). This demonstrates that leg cells can respond to their positions in an antennal imaginal disk in a highly specific manner, by differentiating in particular directions. This is one of the best pieces of evidence for universality of the mechanism specifying position during pattern formation[28].

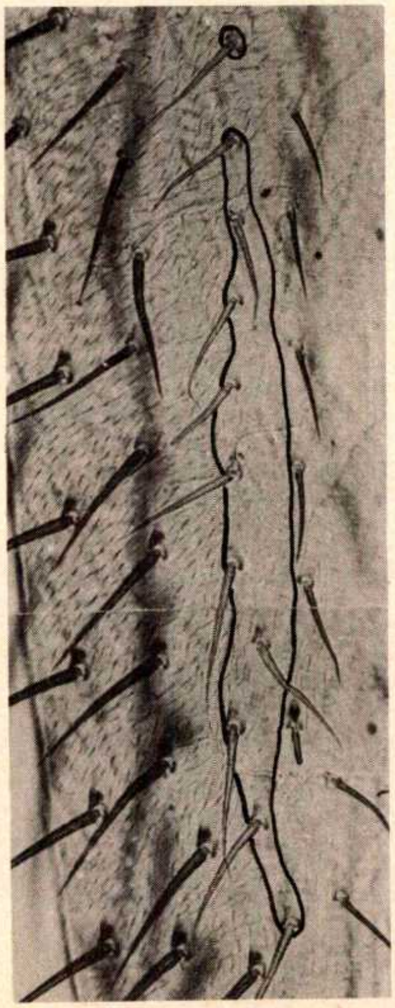

Fig. 4 A *yellow; multiple wing hairs* clone (outline) on the femur of the leg. *yellow* produces pale bristles; *multiple wing hairs* causes the epidermal cells to produce more than the usual one hair per cell. From Bryant and Schneiderman[23].

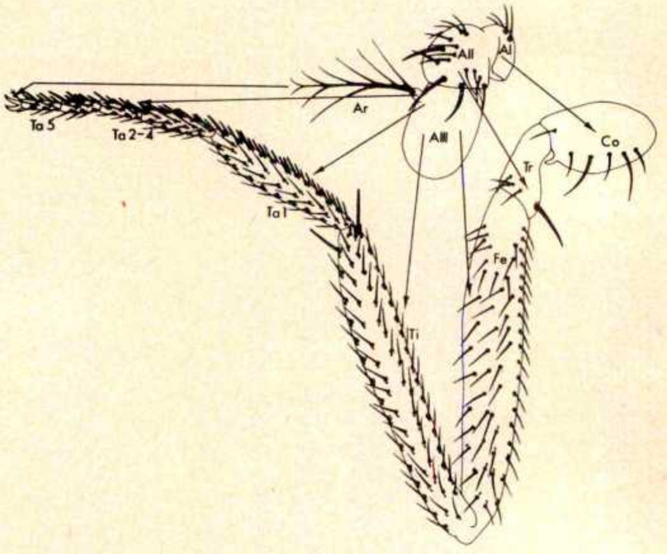

Fig. 5 The correspondence between the structure of the antenna and that of the leg, based on replacements in the leg-antennal intermediates of *antennapedia*. The third antennal segment corresponds not to one but to two leg segments. AI, AII, AIII, first to third antennal segments. Ar, arista. Co, coxa. Tr, trochanter. Fe, femur. Ti, tibia. Ta1–Ta5, first to fifth tarsal segments. From Schneiderman[27] and Postlethwait.

In view of the enormous literature dealing with the development of transplanted fragments of imaginal disks, it is perhaps surprising that much new information could come from the direct surgical approach. It is only recently, however, that the development of specific fragments of disks has been followed in detail, and this has disclosed an intriguing type of developmental organization in these structures. When pieces of a leg disk are implanted into the abdomen of host larvae of the same age, they metamorphose with the host and differentiate into recognizable, though uneverted, parts of the leg. Schubiger[29] has shown that the specific structures which are formed depend on which part of the disk is transplanted, so that he was able to construct a complete fate map of the disk. But more interesting are the experiments in which fragments of the disk are given extra time for growth before metamorphosis, either in an adult or a larval abdomen[30]. In these cases one of two phenomena may occur: regeneration of the missing parts or mirror image duplication of those remaining. Furthermore, the capacity for these two activities is limited to certain regions of the disk. Regeneration is found in fragments containing one specific region, whereas duplication is found in fragments lacking this part. We have obtained similar results (Fig. 6) using a new technique of surgery *in situ* on imaginal disks[31].

We have interpreted these surgical experiments to mean that cells in imaginal disks are graded in their developmental capacities. Cells at any one level in the gradient of developmental capacity can, given the opportunity for growth and cell division, replace only those parts which are normally at lower positions in the gradient. When a disk is bisected, the cells at the two cut surfaces have similar developmental capacities, so that in each half they replace those parts of the system which are at lower levels. This leads to regeneration in one of the halves and duplication in the other. Recent experiments in which imaginal disk cells are killed by X-rays indicate that these gradients of developmental capacity are laid down in the disks at the very beginning of their development (J. H. Postlethwait, personal communication).

Similar theories have been proposed to account for the regenerative behaviour of the legs of other insects[32], so for the first time we can begin to relate studies on imaginal disks of *Drosophila* to studies on the appendages of other insects. Indeed it seems that imaginal disks, although internal during larval life and temporarily relieved of the responsibility to secrete cuticle, retain many of the growth patterns and generative abilities of the appendages of less highly evolved insects.

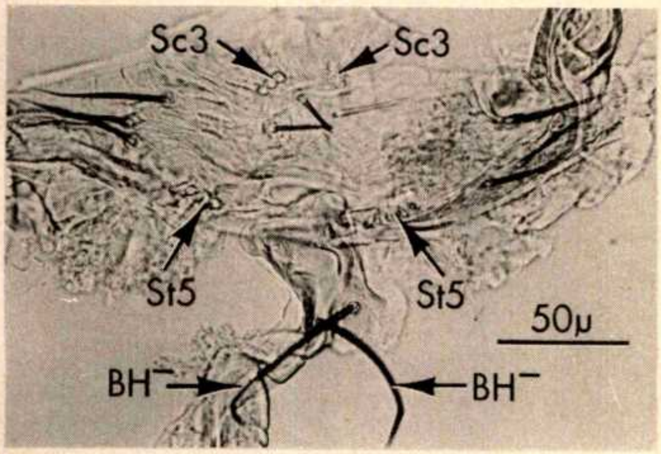

Fig. 6 Mirror image duplication of leg structures, caused by bisection *in situ* of the imaginal leg disk in the larva. Sc3 and Sr4 are specific sense organs of the trochanter, and BH⁻ is a unique bristle of the coxa. From Bryant[31].

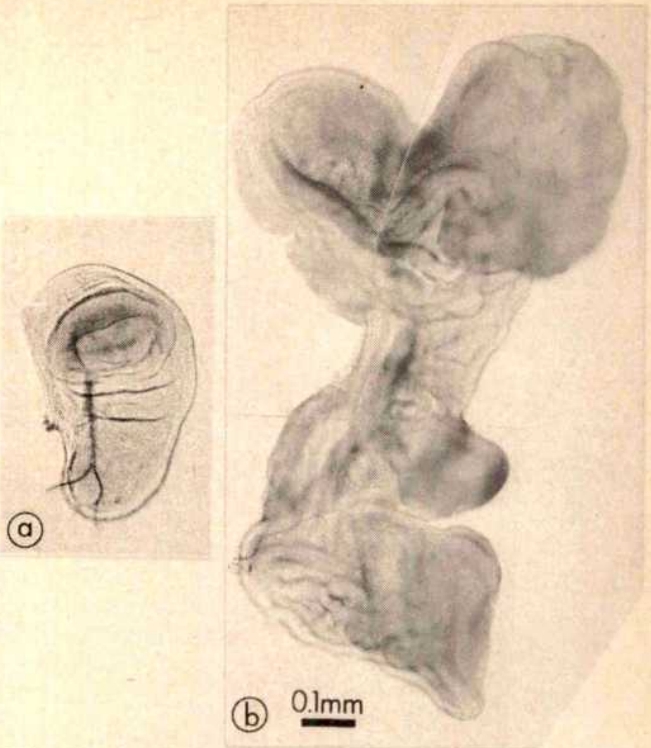

Fig. 7 Wing disks (*a*) from a mature normal larva and (*b*) from a homozygous *l(2)gd* larva 13 days after oviposition. From Bryant and Schubiger[33].

The process of growth regulation and pattern formation in imaginal disks are illuminated in a rather elegant fashion by a new lethal mutant we have isolated in which the imaginal disks undergo spontaneous duplication[33]. The mutant is *lethal (2) giant disks* (*l(2)gd*), and it is characterized by an extreme delay in the initiation of metamorphosis. During the extended larval period, the imaginal disks continue to grow and attain several times their normal dimensions (Fig. 7). The animals die shortly after the initiation of metamorphosis, probably as a result of the inability of these enlarged disks to undergo normal eversion. In mutant leg disks of older larvae not only extra growth but extra folding patterns appear (Fig. 8). Transplantation studies show that the extra folds represent a duplication of the anlagen in the leg disk, so that after metamorphosis two legs are produced instead of one. It is intriguing that the duplicate leg arises in that part of the disk which, as we know from surgical experiments on wild type animals, has the highest developmental capacity. It seems that this mutant in some way liberates a developmental capacity that usually remains latent.

Related to the problem of regeneration in imaginal disks is that of the reconstruction of patterns from dissociated disks[3]. Disks of two genotypes (for example, *yellow; singed* and *multiple wing hairs* leg disks) are mixed, treated with trypsin, and disrupted with a microstirrer. The disrupted disks are reaggregated by centrifugation and, after a short period of culture in an adult, are implanted into host larvae for metamorphosis. After metamorphosis, the implants often include familiar patterns (bristle rows, claw organs and so on) consisting of elements of both genotypes. A widely held view of this phenomenon was that the reconstruction of patterns is achieved by the migration of cells to their preassigned positions in the pattern. Such an intepretation was attractive at a time when the determination of imaginal disk cells was thought to be of a highly specific and rigid nature. But our findings of regenerative capacities in imaginal disks led Poodry *et al.*[35] to re-examine the process of pattern reconstruction. The conclusion from these studies is that directed cell migration is not the

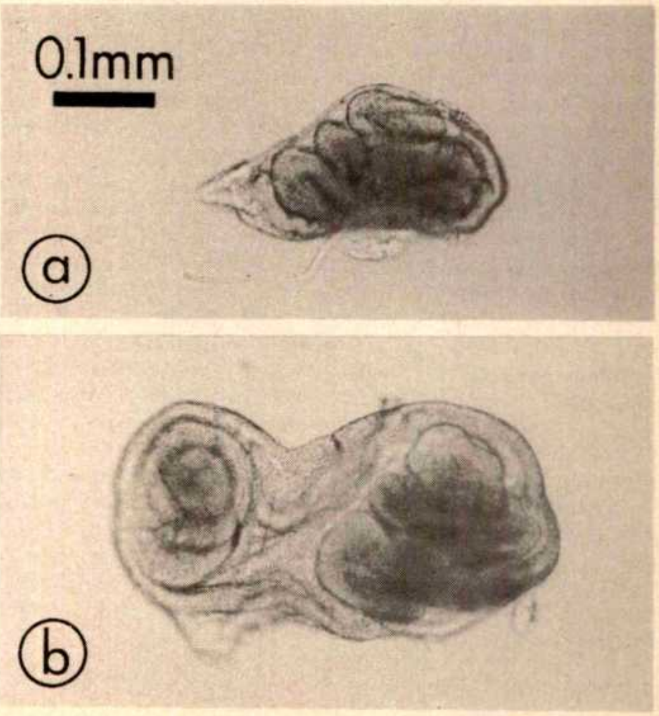

Fig. 8 *a*, Normal leg disk. *b*, Duplicated leg disk from a homozygous *l(2)gd* larva 9 days after oviposition. From Bryant and Schubiger[33].

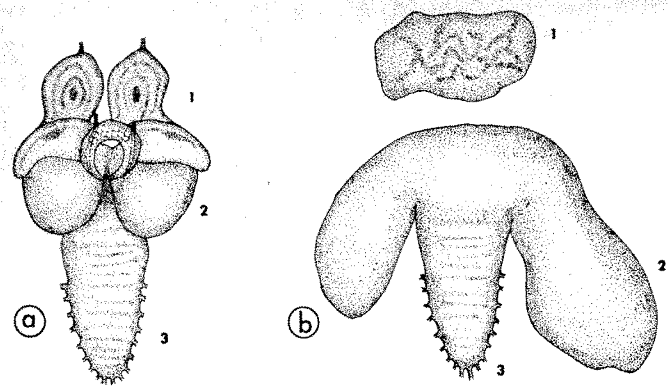

Fig. 9 Brain and eye-antennal disks from (*a*) mature wild type larva and (*b*) homozygous $l(2)gl^4$ larva. In the mutant the optic lobes (2) of the brain are overgrown, and the eye-antennal disks (1) are disorganized and fused. The ventral ganglion (3) appears to be normal. From Gateff and Schneiderman[6].

mechanism for reconstruction, but rather that a considerable amount of "repatterning" occurs in the randomly reaggregated cell population. In our view, pattern reconstruction is a repetition of the events occurring during pattern formation in normal development, and as such can be used as a model system for the investigation of those events.

Transdetermination

It is becoming increasingly clear from many of the recent studies on imaginal disks that these structures are capable of a considerable degree of developmental regulation. Fragments of disks can, when allowed time for growth before metamorphosis, give rise to structures normally formed by other parts of the same disk. But even more remarkable is the ability of disk tissue to give rise to structures normally formed by different imaginal disks, by a process known as transdetermination. This phenomenon has been studied extensively by Hadorn and his collaborators[36], who have employed a technique of serial subculture of disk tissue using adult abdomens as culture chambers. Periodically, the developmental capacities of pieces of the tissue are tested by implanting into host larvae for metamorphosis. A common result from such experiments is that the tissue differentiates "autotypically" into structures characteristic of the disk from which it is derived. For example, tissue derived from a leg disk frequently produces sex combs and claw organs in the metamorphosis test. But the test pieces sometimes differentiate "allotypically" into adult structures other than those for which the donor disk was originally determined, showing that transdetermination has occurred during the growth of the tissue. For example, leg disk tissue was found to produce wings, thorax, antenna and proboscis[29]. In other cases, the tissue became "atelotypic" and completely lost the ability to differentiate into cuticular structures[36].

These discoveries stimulated a number of workers to investigate the mechanism of the alterations. As a result there is extensive information about the developmental capacities of imaginal disk tissue after prolonged *in vivo* culture. It has been shown that the process of transdetermination may occur in populations of contiguous cells rather than in single cells[37]. It has also been demonstrated that the process depends on cell division[38]. The mechanism still remains as elusive as the mechanism of determination itself, however. New methods for culture *in vitro* may provide a new route into the analysis of this phenomenon.

Neoplasms

Insects differ from vertebrates in the almost total absence of neoplasms or cancers. Indeed as late as 1967 not a single lethal, transplantable and invasive neoplasm had been found in any insect. Approximately 400 papers had been published describing tumours in insects, but Harshbarger and Taylor[39] examined the available material and concluded that none of these tumours are comparable with the neoplasms found in vertebrates, a conclusion now shared by most students of the subject. A few of the tumours of *Drosophila* such as those occurring in the *female-sterile* and *fused* mutants[40] show rapid growth of specific cell types but the growths are not highly invasive. We have found that "tumorous head" outgrowths are in fact homoeotic changes in which parts of the head are replaced by parts of abdominal tergites, genitalia, and legs (J. H. Postlethwait, J. H. B. and G. Schubiger, unpublished). "Melanotic tumours" seem to be little more than accumulations of blood cells at various sites[41]. None of these so called tumours is invasive or lethal to the host, nor have any been subcultured as have many of the tumours of vertebrates.

About three years ago Gateff[6] discovered two neoplasms in the mutant *lethal (2) giant larva* ($l(2)gl^4$) of *Drosophila*. One of these is a lethal, malignant, and invasive neuroblastoma of the larval brain (Fig. 9). It can be repeatedly subcultured in adult abdomens for many generations, in which it is also malignant and invasive. It is the first invasive and lethal neoplasm found in invertebrates and it shares many features with malignant neuroblastomas of vertebrates. The second neoplasm found in $l(2)gl^4$ is a lethal but non-invasive neoplasm of the imaginal disks. The imaginal disks of $l(2)gl^4$ larvae are very disorganized (Fig. 9) and fail to metamorphose into cuticular structures when transplanted into normal larvae. When transplanted into adult hosts the $l(2)gl^4$ disks grow rapidly into compact structures and cause the death of the host within 7–14 days. Both neoplasms show histological and morphological changes typical of neoplastic cells in general, such as reduced intercellular contacts, nuclear deformation, and changes of the cell and nuclear membranes.

The discovery of these neoplasms led us to examine the general question of tumorigenesis in insects. We propose that the infrequent occurrence of true neoplasms in insects (in contrast to vertebrates) is a consequence of certain peculiarities on insect development, notably the absence of cell division in most adult tissues and in many larval tissues, the destruction of many larval tissues during metamorphosis, the frequent occurrence of polyploidy and polyteny, and the relative stability of the karyotype. It seems that neoplasms develop in *Drosophila* chiefly as a result of genetic mutations, and that genetically induced neoplasms can be expected to occur in situations where there is rapid cell division, such as in the embryo, and in the imaginal disks and nervous system of the larva.

We have recently begun to look for neoplasms among embryonic lethals, and the results have been encouraging. Gateff (personal communication) has shown that the nervous system of the well known embryonic lethal *Notch* ($Df(1)N^8$) is neoplastic and promptly kills hosts which receive transplants. Unlike the neuroblastoma of $l(2)gl^4$, the *Notch* neoplasm consists not only of neuroblasts but also of other cell types present in the embryonic nervous system. We have also examined several mutants which have defective imaginal disks and brains, and which die during the larval–pupal transformation. One of these, *l(2)gd*, gives rise to a brain neoplasm very much like that of $l(2)gl^4$, but the mutation is at a different locus on the second chromosome[33]. Since it appears that we can induce and select large numbers of mutants which might produce neoplasms in *Drosophila*, we may be able to identify the genetic change responsible for a particular cancerous property. The elucidation of the mechanisms of neoplastic transformations in this system would surely be relevant to an understanding of cancers in other systems. We know of no system in higher organisms in which the genetic changes underlying neoplastic transformations can be examined as easily and in as much detail.

Selection of Mutants

An important approach to developmental problems using *Drosophila* involves the selection and analysis of large numbers of mutants affecting particular developmental or physiological processes. By studying the ways in which mutations can modify these processes, we hope to reach an understanding of the genetic control of the processes in the normal situation. Wright[42] has recently reviewed the progress being made in the application of this approach to particular aspects of embryogenesis. In addition, the development of imaginal disks is being studied in this way in several laboratories. Recently Shearn *et al.*[43] have selected and examined 134 lethal mutants in which death occurs during metamorphosis, and have found that nearly half of them have defective imaginal disks. In some of these, the imaginal disks are absent and in others they are morphologically abnormal. In some other mutants the disks appear morphologically normal, but are unable to metamorphose properly when transplanted into normal host larvae. Stewart *et al.*[44] have been working along similar lines, using a technique for assessing the developmental capacities of the disks *in vitro*.

The experiments on late larval–pupal lethals indicate that the larval organisms can tolerate almost any kind of defect in the imaginal disks including their complete absence. Hence the selection of such mutants should make it possible to analyse rather completely the genetic control of imaginal disk development. The fact that mutations like *l(2)gd* can have profound effects on the disks without impairing the viability or structure of the larva emphasizes the genetic independence of the larval organism and the future imago. One can now investigate the possibility of distinct larval and imaginal gene sets, each capable of separate evolution, as proposed by Wigglesworth[45].

The application of the mutant selection approach can be greatly extended by the use of conditional mutants which show the mutant phenotype in certain (restrictive) conditions and the normal phenotype in other (permissive) conditions. Considerable effort is now being devoted to the collection of two types of conditional mutants in *Drosophila*: those which are temperature sensitive and those which are nutrition sensitive.

Suzuki and his colleagues[46] have recently shown that the use of the powerful mutagen ethyl methane sulphonate (EMS) permits the isolation of large numbers of temperature-sensitive lethal mutants. As a working hypothesis it is assumed that these mutants are of the missense type, and that this leads to amino-acid substitutions in polypeptide chains which render them thermolabile. The conditional nature of these mutants permits the definition, for each of them, of a period of development during which the organism is sensitive to the restrictive conditions (usually high temperature; 29° C). Exposure to such conditions during the temperature-sensitive period results in subsequent death at the "lethal phase", but exposure at any other time permits survival. Hence, the study of these mutants allows the determination of the periods during which certain gene products are necessary for development. Most of the mutants studied have a temperature-sensitive period in the embryonic or late larval–pupal stage, indicating that many gene products come into use for the first time at these stages. This finding is consistent with the intense morphogenetic activities occurring at these times. Arking (personal communication) has now collected more than 100 temperature-sensitive larval–pupal lethals, many of which have imaginal disk defects, and some of which may prove to have endocrine deficiencies.

Nutritional conditional lethals (auxotrophs) have even greater prospective value than temperature-sensitive lethals in the analysis of the genetic control systems of eukaryotes. It is therefore surprising that only a few laboratories have taken up the challenge of producing these mutants. Several defined media have been devised for *Drosophila*, and conventional mutagenesis techniques should permit the isolation of mutants whose survival depends on the addition of supplements to these media. Vyse and Nash[47] were the first to report the isolation of mutants of this type. They produced three auxotrophic mutants, one of which (1308) required RNA for growth. This was later shown to be a requirement for both purines and pyrimidines, presumably as a result of a double metabolic block[48]. A specific requirement of pyrimidines for growth has been demonstrated in the mutant rudimentary by Norby[49]. It is of interest that homozygous females of this stock are sterile, as is the case with several other auxotrophs (D. Nash and D. Falk, personal communication). Thus, female sterility may prove to be a convenient method of preliminary screening for auxotrophic mutants.

The availability of auxotrophic mutants of *Drosophila* will permit us to answer many of the questions which recent findings on microorganisms lead us to ask about higher organisms. We should be able to test whether there is close linkage of genes concerned with particular metabolic pathways; this needs to be settled before we can ask meaningful questions about the regulation of gene activity. Auxotrophs could be used to increase tremendously the resolution attainable in genetic fine structure studies. Furthermore, some technical advances may accrue from these studies. For example, a thymidine requiring mutant would be extremely valuable for DNA labelling. Some of the enzyme deficiencies may prove useful as genetic markers for tracing the cell lineage relationships of the larval organs and of the internal organs of the adult.

Prospects

In this brief survey of *Drosophila* developmental genetics, limitations of space have precluded the discussion of several key areas, such as the current intensive efforts to understand spermatogenesis[50], oogenesis[40], the control of genetic activity in polytene chromosomes[51] and the developmental genetics of behaviour[52,53]. Nevertheless, we hope to have conveyed an idea of some of the approaches being made toward an understanding of the development of *Drosophila*.

Clearly many of these approaches have only begun to be exploited. Somatic crossing over makes possible the introduction of mutant cells into developing embryos at specific stages of development and permits studies of the interaction of mutant and wild type cell populations. The use of this method to investigate the processes of intercellular communication which underlie pattern formation[54] still has great potential. The use of temperature-sensitive mutants and of somatic crossing over techniques shows great promise as general techniques for investigating the time of action of genes and gene products during development[46,55]. The great improvements in cytoplasmic and nuclear transplantation techniques for *Drosophila* and the use of laser microbeams to alter the fundamental organization of the egg and embryo also hold immense promise. And underlying all of these are the six decades of intensive genetic work which now enable experimenters to dissect the development of *Drosophila*, gene by gene.

In the next few years we expect at least one important technical advance to be made in *Drosophila* developmental biology, and that is the perfection of techniques for culture *in vitro*. Until recently, only limited success had been reported with *Drosophila* tissue culture, but many workers have now reported encouraging results with cells from embryos[56,57]. In fact, Schneider (personal communication) has now been able to culture cells which will metamorphose into adult structures when transplanted to host larvae. Such techniques will permit the long awaited biochemical analysis of many of the problems in the developmental genetics of *Drosophila*.

We thank colleagues whose traditions of cooperation and sharing of stocks and information make this field a joy to work in, and especially our co-workers in the Developmental Biology Laboratory and Center for Pathobiology for helpful discussions and suggestions. Research from our laboratory described in this report was supported by grants from the US National Science Foundation, the American Cancer Society, and the US National Institutes of Health.

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MOLECULAR BIOLOGY

Reverse Transcriptase, the DNA Polymerase of Oncogenic RNA Viruses

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The excitement aroused by the idea that transformation of cells by RNA tumour viruses might depend on the activity of a reverse transcriptase enzyme(s) specific to the virus has stimulated much research since the enzyme was discovered in 1970. But the questions of the physical identity and catalytic activities of the enzyme(s), its function in transformation and whether it is unique to RNA tumour viruses remain unanswered.

TEMIN's enzyme is now one of the most discussed and utilized elements in tumour virology and there is no need to go deeply into the history of his provirus theory[1,2], which led to the search for and discovery of this enzyme[3-9]. Briefly, Temin proposed in 1964 that the genome of an RNA tumour virus must be transcribed into DNA (the "provirus"). His speculation was made to explain how an RNA virus produced a stable genetic trait, a characteristic passing from cell to daughter cell (namely neoplastic transformation). The DNA provirus in a double stranded form could then be integrated into host cell DNA. The discovery of the enzyme led to an extraordinarily rapid collection of information on its properties and on its distribution in tumour viruses[10-12] so that now it is virtually a marker for a transforming RNA virus.

The virion reverse transcriptase may be essential for viral replication and cell transformation but these points have not yet been established conclusively. Initially, indirect experiments indicated that RNA tumour virus replication required a DNA intermediate (virus specific)[13-16]. The subsequent discovery of DNA polymerases in all known RNA tumour viruses (see refs. 7 and 12 for recent summaries) and its apparent ability to transcribe all the viral RNA[17] are in keeping with the role of this DNA polymerase in viral replication and cell transformation. Two approaches have been utilized to try to provide more direct evidence of the enzyme's requirement. The first approach has been the use of mutants. Hanafusa[18] isolated a mutant of RSV called RSV$_\alpha$ (O), which is non-infectious, cannot transform chick fibroblasts, and does not contain polymerase activity. The addition of an avian leucosis virus (ALV) (which replicates in but does not transform these cells) with RSV$_\alpha$ (O) resulted in transformed fibroblasts. The obvious interpretation is that inability of RSV$_\alpha$ (O) to replicate and transform chick cells is due to a mutation in the gene(s) specifying reverse transcriptase; in the presence of ALV, the RSV$_\alpha$ (O) is able to use the ALV enzyme and thereby is capable of transforming cells (phenotypic complementation). Ultimately, non-infectious virus was produced by the transformed cells and the obvious interpretation is that the polymerase is required for transformation but not maintenance of the transformed state. It has not been satisfactorily demonstrated, however, that the sole or primary effect in this mutant is on the reverse transcriptase, and the biochemical evidence for defective or absent enzyme was not definitive. For example, results from mixing experiments with mutant and wild type enzyme are consistent with the presence of an inhibitor in the mutant preparation. Further, DNA polymerase activity was recently found in a similar mutant[19]. It will be necessary to study several mutants and provide more detailed biochemical analysis of any detectable polymerase before definitive conclusions can be made on questions relating to the necessity of reverse transcriptase for initiation of transformation and for maintaining the neoplastic state. The second approach has been the use of inhibitors, rifamycin derivatives[20–23], and streptovaricins[24]. Streptovaricins, which are fair reverse transcriptase inhibitors, were reported to block transformation of mouse fibroblasts by MSV, and the inhibition did not seem to be due to toxic effects on the cells[25]. The MSV effects on mouse fibroblasts, however, are measurements of viral replication rather than transformation[26]. Therefore, the interpretation of these results should be limited to supporting the notion that the enzyme is required for viral replication, and the limitation of this conclusion is the possibility of non-specific inhibition.

More than 200 rifamycin derivatives have been studied for their effect on the viral and on purified cellular DNA polymerases[23]. A spectrum of derivatives is available, ranging from ineffective to extremely potent inhibitors. After pretreating virus (MSV) with different derivatives and then removing the compound (so that toxic effects on cells do not obscure the results), a direct correlation was found between inhibition of reverse transcriptase and loss of the capacity to transform rat cells (R. C. Ting, S. S. Yang and R. C. G., in preparation). Again, an argument can be made that factors essential to viral replication and transforming capacity other than the polymerase are also affected by the rifamycin derivatives, and coincidentally the inhibition of these factors parallels inhibition of the polymerase.

One problem is that some of the biochemical evidence does not favour a replicative function for the reverse transcriptase. For example, the size of the DNA pieces made is small; the amount of DNA synthesized relative to input 70S RNA is low, most of the DNA is produced from a relatively small region of the 70S RNA[27–29]; and most recently Wells *et al.* (unpublished work of R. D. Wells, R. M. Flugel, J. E. Larson, P. F. Schendel and R. W. Sweet) have shown that the AMV enzyme, like other known DNA polymerases, does not effect *de novo* initiation of a new DNA strand in templated reactions. These problems may, however, be peculiar to the *in vitro* systems used to study DNA polymerases; and the combined biological evidence strongly suggests that reverse transcriptase is the enzyme for replication of these viruses.

Properties of the "Purified Enzymes"

The enzymes from avian type C viruses, purified (AMV)[30] and partially purified (RSV)[31], have molecular weights of about 110,000 and, at least in the case of AMV, a second protein of 69,000 molecular weight is present. In contrast, a molecular weight of 70,000 was reported for the partially purified enzyme from RLV[32]. Whether a true physically important difference exists between avian and mammalian reverse transcriptases to account for this difference, or whether there is a more trivial explanation, awaits further studies.

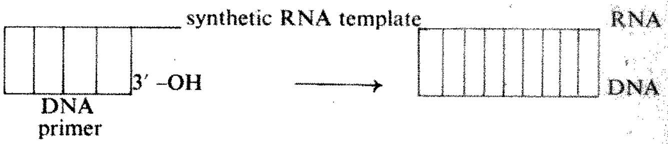
In a recent report it was concluded that the RNA and DNA template activities of reverse transcriptase were separate (two different enzymes)[19], but this has not been the experience of others[30,33]. Partially purified[33] and highly purified[30] enzymes have been found to retain the RNA, RNA–DNA hybrid, and DNA template activities, and competition experiments have shown that 70S RNA, RNA–DNA hybrids, and DNA compete with each other for the purified polymerase, supporting the view of one catalytic template site[7,33]. Presumably then the one enzyme can carry out the following 2-step synthetic sequence:

Viral RNA $\longrightarrow$ RNA–DNA hybrid $\longrightarrow$ double stranded DNA

The double stranded DNA may then be integrated into the host cell DNA and when "turned on" may transcribe viral RNA molecules.

The template function of exogenous 70S viral RNA (with enzyme partially purified and separated from its own 70S RNA) merits further comment. Exogenous 70S RNA has so far been shown to template only with DNA polymerases of the avian viruses, RSV[33] and AMV[30]. In similar assay conditions, activity has been considerably lower with the purified polymerases from the type B monkey mammary tumour virus and with RLV using 70S RNA from RLV or AMV. Lack of acceptance may be due to differences in enzyme primer requirements, template specificity, or low levels of contaminating RNAase. This is a particularly critical point with respect to negative results with cellular DNA polymerases and 70S RNA template activity.

The purified (or "crude") viral DNA polymerase does not accept single stranded synthetic homopolymeric RNA unless accompanied by a complementary oligonucleotide primer[35]. The DNA synthesized with the template-primer complex is covalently joined to the primer[29,35], and the primer-product hydrogen bonded to the template RNA as shown below.



Recent experiments by Verma *et al.*[35], Wells *et al.* (unpublished), and Hurwitz (personal communication) have shown that the viral RNA may be both template and primer. The DNA product synthesized with a partially purified AMV DNA polymerase and exogenous AMV 70S RNA is covalently bonded to the viral RNA, perhaps as shown as mechanism 2 in Fig. 1. On caesium sulphate density gradient centrifugation (which separates RNA, DNA, and RNA–DNA hybrids) the labelled DNA product could not be separated from the viral RNA by heat denaturation. After alkaline hydrolysis (or RNAase) and heat, the product moved to the DNA region (J. Hurwitz, personal communication). These and other[29,36] experiments have convincingly indicated that a covalent bond joins the DNA product to a template-primer RNA. At first glance these results appear to be at odds with earlier reports[10] which indicated that after only heat denaturation the product moved from the hybrid to the DNA region. In the earlier reports, however, the whole viral "system" was utilized (disrupted virions with its endogenous RNA instructed synthesis of DNA), and these systems may have included an endonuclease. In the studies reporting evidence for the covalent bond, the enzymes were partially purified and the response to exogenous RNAs investigated. An endonuclease may therefore have been removed.

Potential Uses

(1) If reverse transcriptase is specific for RNA oncogenic viruses it is obvious that when appropriately assayed a positive result will support the notion that a particle is an RNA virus and at least suggests that the particle might be oncogenic. Every known oncogenic RNA virus tested so far contains this enzyme activity. This approach has already been utilized in two recent preliminary reports on human particles. (*a*) Reverse transcriptase is present in particles from human milk obtained from women with a familial history of breast cancer and from inbred populations[36]. In this case there was some uncertainty that the particles were true viruses because they had not been grown in tissue culture and morphological studies were handicapped by other components in human milk. The evidence that these specimens contain reverse transcriptase considerably advances the notion that the particles are viral and potentially oncogenic. (*b*) The ESP-1 virus isolated from cells from the pleural fluid of a child with lymphoma and successfully grown in tissue culture by Priori *et al.*[37] contains reverse transcriptase[38]. Because it was replicating in culture and could be carefully evaluated morphologically, no further evidence was really needed to show that the particle was indeed a budding RNA virus. In this case, the presence of the enzyme supports the concept that the virus may be oncogenic and further provides a tool for subsequent hybridization experiments (see below) that may more directly help to evaluate whether this or a similar virus actually plays a role in the pathogenesis of human tumours. It has not been proved that ESP-1 virus is of human origin[39], but the properties of the viral enzyme may help to clarify this point. The data which are required are: first, a careful comparison of the biochemical and immunological properties of the purified enzyme with the polymerase of the virus in question. The enzyme resides in virion cores, and therefore should not be subject to changes dictated by the recipient cell; second, by making labelled DNA copies of the respective viral RNA genomes (in this case murine and ESP-1) with their polymerases one can then compare the degree of hybridization of the DNA with the respective viral RNA as well as to cellular RNA (mouse and human). At present no definitive conclusion can be reached about the origin of ESP-1. (2) The enzyme may be useful for preparing highly radioactive DNA for hybridization studies. The DNA product of the endogenous RNA instructed reaction can be used to look for complementary sequences with cellular RNA. (3) Reverse transcriptase assays have been increasingly helpful as a rapid and sensitive method for identifying and quantitating known RNA tumour viruses. For an unambiguous measurement, contamination with cellular DNA polymerases should be slight (see below). The lower limits of sensitivity in most laboratories appear to be around 10^2–10^3 infectious units which is much more sensitive than electron microscopy.

Criteria

Even with best purification methods, however, cellular enzymes, including DNA polymerases, may contaminate viral preparations, and some minimum criteria are therefore needed for establishing the presence of "reverse transcriptase" in a virus or suspected virus. (*a*) The particle in question should be shown to band at the appropriate region in a sucrose gradient (approximately 1.16 g ml.^{-1} for the type C viruses and somewhat higher for the type B), and the DNA polymerase activity must be in the same region. If virus is pre-treated with an appropriate concentration of non-ionic detergent, viral nucleoids (cores) are liberated and these band at a higher density (approximately 1.25 g ml.^{-1}) . As originally shown by Gerwin *et al.*[40] the polymerase will then band with the core. Higher concentrations of detergent (or high salt) may completely liberate the enzyme from other viral components so that the enzyme is now "free" at the top of the gradient. (*b*) The polymerase assays should initially include endogenous synthesis of DNA. This activity should be RNAase sensitive, require disruption of the virus, and require the presence of all four deoxynucleotides and magnesium. The conditions for RNAase sensitivity are of some importance. High RNAase concentrations with no salt will degrade double stranded RNA or RNA of RNA·DNA hybrids. It would be preferable to show sensitivity with relatively low RNAase concentrations (10–20 µg ml.^{-1}) and high salt (0.2 M). In these conditions most RNA hybridized to DNA should not be susceptible to RNAase. Sensitivity to RNAase can then be assumed to result from degradation of single stranded RNA, a more specific template for viral polymerase than DNA·RNA hybrids (see below). (*c*) Analyses of the product should include proof that the product is DNA and that at some point in synthesis the DNA is hybridized to RNA. Most investigators have shown this with equilibrium centrifugation in caesium sulphate density gradients. DNA products of early synthesis band in the RNA region. With increasing time of incubation the product moves to the region characteristic of DNA[10,41]. The most definitive evidence for a viral reverse transcriptase is that the DNA product specifically hybridizes to viral 60–70S RNA. Again, this is generally carried out by equilibrium centrifugation after initial isolation of the DNA product, removal of RNA, and hybridizing the DNA back specifically to the viral RNA. (*d*) Exogenous templates, antibodies, and inhibitors are useful in preliminary detection of the viral enzyme and in proper combination they may provide a rapid and easy assay which is reasonably conclusive.

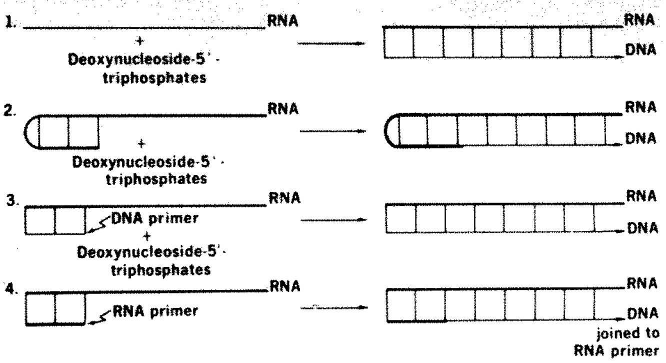

1.
RNA
+
Deoxynucleoside-5'-triphosphates
RNA
DNA
2.
RNA
+
Deoxynucleoside-5'-triphosphates
RNA
DNA
3.
RNA
DNA primer
+
Deoxynucleoside-5'-triphosphates
RNA
DNA
4.
RNA
RNA primer
RNA
DNA
joined to RNA primer

Fig. 1 Schematic illustration of possible biochemical mechanisms for step 1 (RNA → DNA) of viral reverse transcriptase. In mechanism 2 the 70S RNA has a complementary region with free 3'-OH and which acts as the primer for synthesis of DNA directed by the remaining RNA template. Mechanisms 3 and 4 would add importance to small RNA and DNA molecules that may be present in the virus.

Synthetic Templates

The viral enzyme has relative affinity for double stranded synthetic homopolymers containing one polydeoxyribonucleotide strand and one polyribonucleotide (for example, poly dT·poly rA and poly dC·poly rG)[11]. Enhancement of sensitivity of detection has made them useful in preliminary searches for the viral enzyme as initially advocated by Spiegelman[42]. It is quite clear, however, that these polymeric hybrid templates are not specific. Every purified DNA polymerase investigated, including those from *E. coli*[34,43], *Micrococcus luteus* (unpublished work of R. D. Wells, R. M. Flugel, J. E. Larson, P. F. Schendel and R. W. Sweet), normal fresh blood human lymphocytes (R. G. Smith and R. C. G., in preparation), normal mammalian cells in tissue culture[44], and calf thymus[43], accepts these templates very well. Even in preliminary surveys their usefulness may be limited. For example, some crude preparations of virus or virus heavily contaminated with Mycoplasma have shown minimal response. This was true with the polymerase from two potential candidates for human tumour viruses, the milk particles[36] and ESP-1[38], and is probably due to nucleases. Baltimore compared template preferences of DNA polymerase I of *E. coli* and the AMV enzyme[34]. He concluded that although the *E. coli* enzyme will "read" off the ribohomopolymer strand of a hybrid template, it has marked preference for the deoxyribohomopolymer strand. Comparing the DNA polymerases of AMV, *E. coli*, and *M. luteus*, Wells *et al.* (unpublished) find for all three: (*a*) there is preference for double stranded polynucleotides (DNA preferable to RNA); (*b*) DNA–RNA hybrid polymers are suitable template (primers); and (*c*) double stranded synthetic RNAs serve (but poorly). In short, there was little if any selective acceptance of polymeric duplex templates with AMV compared with bacterial DNA polymerases. Natural RNA templates were not studied.

Templates that Distinguish

Combinations of synthetic primer oligomers with homopolymeric templates (with excess template to primer) allow one to distinguish the viral enzyme from other DNA polymerases. This is particularly true with oligo dT·poly rA and oligo dT·poly dA with TTP as substrate. For example, with the AMV enzyme oligo dT·poly rA is about 50 to 100 times more active than oligo dT·poly dA[44]. Conversely, the DNA polymerases of *E. coli*[29,34,47], *M. luteus*[29], calf thymus[46], and normal human lymphocyte DNA polymerase I and polymerase II (R. G. Smith and R. C. G., in preparation) all show marked preference for oligo dT·poly dA.

Viral and the principal mammalian and bacterial DNA polymerases can also be distinguished with natural RNA templates, in particular the single stranded viral 70S RNA. Although 70S viral RNA is not as effective a template as some of the synthetic DNA and DNA·RNA hybrid templates or natural "activated" DNA it will work with the viral enzyme but to a relatively small degree or not at all with other tested DNA polymerases[43]. It is apparent then that the appropriate use of templates may distinguish between purified viral and cellular enzymes. It should be noted, however, that enzymes that may be viral in origin may not give the appropriate template response if significantly contaminated with nucleases.

Antibodies

Aaronson *et al.* have obtained antibodies against viral (mouse) reverse transcriptase[45]. The antibody has cross-reactivity against the polymerase from some mammalian type C RNA viruses, for example, cat, rat and hamster, but not against polymerase from avian type C or any "type B" RNA virus[46]. The antibody did not cross-react with two major DNA polymerase activities from tissue culture cells, so it was proposed[33] that this antibody could be used to ascertain if any DNA polymerases found in human leukaemia were from mammalian leukaemia virus. This approach is based on several assumptions. (1) The two activities found in normal cells are assumed to represent the only DNA polymerases, that is, that no polymerase was missed in isolation attempts. In view of the very late discovery of DNA polymerases II and III in *E. coli*, this cannot be taken for granted. (2) That two activities represent two separate DNA polymerases. The evidence for two proteins was two separate activity peaks on columns. Because these were not highly purified enzymes and protein peaks were not shown in their report, this could represent one DNA polymerase contaminated by activators and inhibitors that vary in their column elution and account for spurious peaks. (3) Antibody may have been directed against adventitious factors required for maximum polymerase activity rather than against the polymerase. These factors may not be required to the same degree for an enzyme of another source. This is a serious pitfall when antibody is prepared against proteins not purified to homogeneity. (4) Finally, and most significant, it is assumed in this approach that an antibody to a mouse viral enzyme will cross-react with a potential human viral enzyme. Since cross-reactions were not found with type B virus, a putative human leukaemia virus would have to be of the C type. In any event, recent information[47] indicates that the mouse antibody did not cross-react with the polymerase from a newly isolated type C monkey virus. The lack of applicability of this mouse antibody approach to human tissues is now clear.

Inhibitors

There have been several reports of inhibition of reverse transcriptase by various compounds, particularly rifampicin derivatives[20–23,48], streptovaricins[24], ethidium bromide, daunomycin, and related compounds[49,53] and most recently poly rU[51]. What are needed, of course, are specific or relatively specific inhibitors. This would greatly help in answering important biological and biochemical questions. Initially, Green and his associates[20] reported specificity for N-demethylrifampicin and the dimethyl benzyl derivative of rifampicin for the viral enzyme. Unfortunately, N-demethylrifampicin is not a very potent inhibitor[20,23,48], but it has in other hands also been somewhat specific for RNA directed DNA synthesis[23]. The specificity of the dimethylbenzyl derivative has not been extended. It is, for example, a potent inhibitor of purified DNA polymerases from normal human lymphocytes[23]. Some streptovaricins, similar to the findings with N-demethylrifampicin, although not very potent, appear to give a range of some selectivity for RNA directed reactions[23]. Ethidium bromide and daunomycin offer little if any specificity. Recently, poly rU was reported to selectively inhibit reverse transcriptase, and it was proposed that it might be used as a rapid and simple approach for differentiating cellular and viral enzymes obtained with crude extracts[51]. Although these results have been confirmed[52], some other viral polymerases were inhibited much less than RLV, and two highly purified DNA polymerases from normal human lymphocytes were inhibited at least as strongly as any viral polymerase[52], so it is clear that this approach may not be very useful.

Reverse Transcriptase in Cells

Last year an RNA dependent DNA polymerase in some human acute leukaemic cells was described[21]. This was the first report of this activity in a mammalian cell, and it was based on response to both natural and synthetic templates. The response to natural RNA was shown to be RNAase sensitive[21,48], resistant to actinomycin[53], and sensitive to N-demethylrifampicin[21,48,53]. Spiegelman and his associates simultaneously found much greater activities with certain synthetic templates with virtually all neoplastic cells compared with normal cells, and proposed a potential prognostic and/or diagnostic use of these templates[43,54]. Neither of these studies, of course, clarified the origin of these activities, and the point was stressed that, whether viral or cellular, differences in activities between normal and neoplastic cells which potentially might be involved in reversal of information flow could account for variation in RNA species between these cells[21,49]. It was already known that the DNA polymerase from *E. coli* accepted the synthetic double stranded RNA, poly rA·rU[55], but no "natural" (cellular or viral) RNA templates were ever included. Subsequently, "RNA" dependent DNA polymerase activities were described in a number of mammalian cells and in leukaemic sera based on the response to synthetic polymeric templates, especially ribohomopolymer·deoxyhomopolymer hybrids (for example, poly dT·poly rA) or DNA[47,56–58]. As described above, poly dT·poly rA was later shown to lack specificity. Later a DNA polymerase activity from normal cells with a natural RNA (commercial yeast RNA) was reported[59]. This RNA, however, is contaminated with DNA and the response was not shown to be RNAase sensitive; and almost simultaneous with the report on human leukaemic cells, the *E. coli* enzyme was reported to utilize cellular RNA[60]. This reaction was shown to be RNAase sensitive at high RNAase concentrations in the absence of salt. As discussed above, under these conditions double stranded RNA and RNA of RNA–DNA hybrids (as well as single stranded

RNA) will be RNAase sensitive. Thus, in most studies, unequivocal proof of RNA-directed DNA synthesis had not been demonstrated. This is especially true now that it is known that RNA may act as an initiator (primer) for a DNA polymerase since a primer rather than a template may be destroyed by RNAase treatment. Further approaches are needed; and attempts have now been made to look at cells for ribonucleoprotein particulate fractions that carry out endogenous synthesis of DNA, and which are sensitive to RNAase (in conditions that should degrade only single stranded RNA), which allow appropriate product analysis. Activity has been found by Coffin and Temin in non-virus-producing but RSV-transformed rat cells and much less activity in the non-transformed culture cells[61]. Preliminary evidence has also been reported of similar particulate fractions in tissue culture in a leukaemic cell line which contained visible viral-like particles[62], and recently in some fresh human leukaemic blood cells and in chick embryos (P. Sarin, M. G. Sarnagadharan, R. G. Smith, J. Battacharyya and R. C. G., in preparation). As well as RNAase (10 µg ml.$^{-1}$; 0.2 M NaCl) sensitivity, the DNA product of an early reaction from the leukaemic pellet was shown to band in Cs_2SO_4 in the RNA region[64]. The conditions of sensitivity to RNAase suggest that if the RNA is only a primer hybridized to DNA it must be very small (fewer than ten nucleotides), yet the Cs_2SO_4 and subsequent velocity gradient analyses indicate that the RNA is large. These results, combined with the previous data, suggest that the reaction in leukaemic cells is RNA directed.

Future Problems

Some of the questions which need early answers are the following. (1) What are the detailed biochemical mechanisms for this enzyme? Are they exactly the same as *E. coli*, always requiring free 3′-OH ends and a primer? (2) What is the nature of the primer in biological situations? Is it RNA, DNA, or both? (3) Are there specific primers for different RNA viruses? (4) Does the enzyme physically differ between type B and type C RNA virus groups? (5) Does the enzyme in viruses from higher forms differ from that of lower animals? (6) Can true *in vitro* replication be accomplished? Are there factors the absence of which gives repair synthesis rather than replication? (7) Are any of the DNA polymerases of neoplastic cells, particularly human, viral in origin (in the absence of whole virus)? (8) Do these or similar cellular polymerases carry out true reversal of information flow in biological situations other than neoplastic transformation? (9) Finally, definitive evidence is still needed to prove a requirement of the viral enzyme for initiation of neoplastic transformation, and more evidence is needed to conclude that it is not required for maintenance of transformation.

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Quasi-stellar Objects and Gravitational Lenses

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The space density of gravitational lens images as a function of redshift is calculated for various cosmological models. One cannot interpret all QSOs as gravitational lens images, unless there is a substantial amount of evolution with z in the sources of the lens images, and also a large fraction of the mass of the universe in the form of compact dark objects.

A conservative estimate, assuming no evolution of the sources, and a smoothed-out density of 7×10^{-31} g/cm^{-3}, for the objects which act as lenses, results in a discrepancy by a factor $\sim10^4$ between the comoving density of lens images and QSOs, out to a redshift of $z\simeq2.8$.

MANY people have looked into the possibility of observing the gravitational lens effect. Zwicky[1,2] showed that galaxies offer a much better chance than stars for the observation of this effect, and Barnothy and Barnothy[3] have suggested that QSOs may be distance Seyfert galaxies the intensity of which has been enhanced by the gravitational lens mechanism.

Following Refsdal[4,5] I consider a small source S at a redshift $z=z_s$, and a mass B acting as a gravitational lens at $z=z_b$. The image seen by the observer at O (Fig. 1) consists of two thin crescents which merge into an annular ring when the observer, lens, and source are perfectly aligned. A detailed study of the shape of the lens images has been carried out by Liebes[6]. The important angles involved are: β, angle between lens and source; α, angular separation of images; α_0, the value of α when $\beta=0$.

The total amplification, A, is given by

$$A=\frac{1}{2}\left(\frac{\alpha}{\beta}+\frac{\beta}{\alpha}\right) \qquad (1a)$$

where

$$\alpha^2=\alpha_0^2+\beta^2 \qquad (1b)$$

If, before magnification, the source subtends an angle u, then equation (1) is only valid for $\beta\gg u$. For $\beta\lesssim u$ (in which case the image is an annulus)

$$A\sim\frac{\alpha_0}{u}=A_0$$

If the mass of the lens is M, then

$$\alpha_0^2=\frac{16\,GM\,H_0}{C^3}\;\frac{z_s-z_b}{z_s\,z_b}\;\frac{1+z_b}{\mathrm{T}\,(z_s,\,z_b,\,\text{model})} \qquad (2)$$

$T(z_s,\,z_b,$ model) is a function of order unity depending on z_s, z_b, and the cosmological model, which has been calculated by Refsdal[5], G is the gravitational constant, c is the velocity of light and H_0 is Hubble's constant (which we take throughout as 100 km s/Mpc).

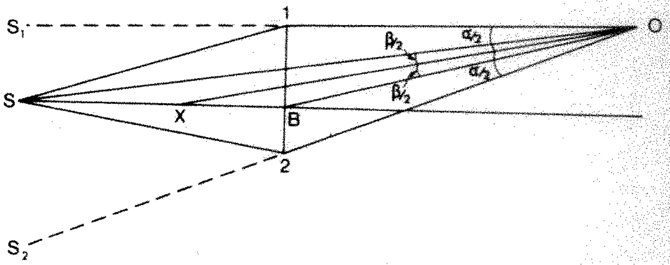

Fig. 1 Diagram showing two light rays S10, S20 from the source S to the observer O which are deflected by the gravitational lens at B. The line XO is a line of symmetry, and S1, S2 are the gravitational lens images.

Fig. 2 shows the amplification as a function of β. For any A_0 and u, the graph of $\frac{A}{A_0}$ against $\frac{\beta}{u}$ is the same shape. A_0 is the maximum amplification and occurs when the source lens and observer are perfectly aligned. Large magnifications are only possible if the unmagnified angular size of the source is small.

Space Density of Lens Images

The probability that a random source in the sky is aligned to within an angle β with a given object is, for small β,

$$\text{probability}=\frac{\beta^2}{4} \qquad (3)$$

If $N(z_s)$ is the number of lenses out to a redshift z when the fraction of objects aligned to within an angle β of a potential lens is

$$\chi\,(z_s)=\frac{\beta^2}{4}\,N\,(z_s) \qquad (4)$$

the magnification A is related to β by

From (1*a* and *b*)

$$\beta^2 = \frac{\alpha_0^2}{2\,(A^2 - 1 + A\sqrt{A^2 - 1})} = \frac{\alpha_0^2}{4\,P(A)} \tag{5}$$

where

$$P(A) = \frac{1}{2}(A^2 - 1 + A\sqrt{A^2 - 1}),\ A \ll A_0 \tag{6}$$

From (2) we thus have

$$\chi\,(z_s, A) = \frac{GMH_0}{c^3\,P(A)}\ \frac{z_s - z_b}{z_s\,z_b}\ \frac{(1 + z_b)\,N(z_s)}{T\,(z_s, z_b, \text{model})} \tag{7}$$

$\chi(z_s, A)$ is the ratio of images (magnified by more than A) to sources, as a function of redshift.

I simplify (7) by taking a mean value of

$$\left\langle \frac{z_b}{z_s} \right\rangle = j = 3/4$$

This is a "round" number which is probably not far from a true average value. The expressions χ and T are insensitive to z_b/z_s.

For small z_s,

$$N\,(z_s)\ \alpha\ z_s^3, \text{ and } T = 1$$

$$\therefore \chi\alpha \left(1 + \frac{3}{4} z_s\right) z_s^2 \tag{8}$$

The number of lens images out to redshifts z_s is given for $z_s \ll 1$ by

$$N_L\,(z_s)\ \alpha\ z_s^5 \left(1 + \frac{5}{8} z_s\right) \tag{9}$$

Putting $z_b = 3/4\ z_s$ in (7) and dropping the suffix s, we obtain for all z

$$\chi = \frac{G\,M\,H_0}{3c^3 P(A)}\ \frac{(1 + 3/4\ z)}{z}\ \frac{N(z)}{T} \tag{10}$$

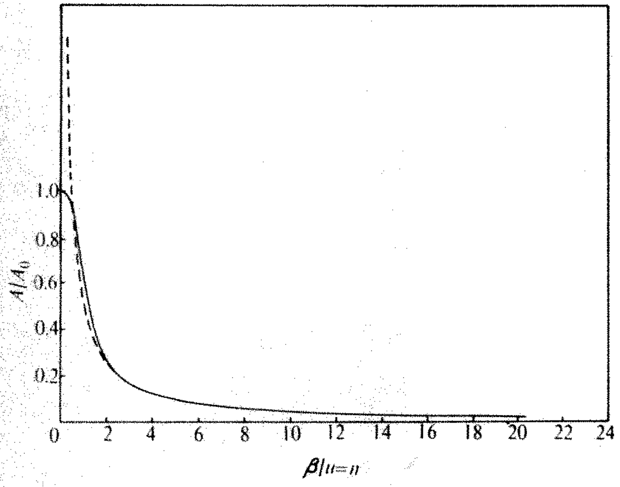

Fig. 2 The ratio of amplification to maximum amplification as a function of $\frac{\beta}{u} = n$. Also shown is the curve $\frac{A}{A_0} = \frac{1}{2n}$ which is a good approximation for $1 < A < 0.9\ A_0$.

Galaxies as Gravitational Lenses

I now consider whether extended objects like galaxies can indeed act as effective lenses. For a lens mass of, say, $10^{11} M_\odot$ at a redshift of $z = 0.75$ with a source at a redshift $z = 1$, the impact distance of the light ray from the centre of the lens is 2.1 kpc ($q_0 = 1$ model). Because a typical galactic radius is ~10 kpc, we must allow for the fact that the light rays pass inside the galaxies.

In this section I work out the effective mass of a galaxy, that is, the equivalent point mass which gives rise to the same deflexion as the galaxy. The effective mass of a galaxy is a function of the impact parameter of the light ray. I take the galaxies to be axially symmetric, and the effective mass $M(r)$, which contributes to the deflexion of the light ray, to be the mass within a cylinder of radius r and axis parallel to the light ray.

For a particular galaxy the impact distance d is the solution of

$$d^2 = \frac{3G}{H_0 c} Y^2\,M\,(d) + \frac{\beta\,c\,z'\,(z_b, \text{model})}{H_0}\,d \tag{11}$$

where

$$Y = z'\,(z_b, \text{model}) \left(\frac{1 + 3/4\ z_s}{z_s\ T}\right)^{1/2}$$

and

$$\frac{c\ z'\ (z, \text{model})}{H_0}$$

is the ratio of the linear to angular size of a rigid rod at a redshift z. To estimate the typical effectiveness of galaxies as lenses, we consider a source at $z_s = 1$ in a $q_0 = 1$ cosmology. The impact distance d is for $\beta = 0$ the solution of

$$d_{\text{kpc}} = 2.12 \left(\frac{M\,(d)}{10^{11} M_\odot}\right)^{1/2} \tag{12}$$

For any other model, and for any other z value, we solve

$$b\ d_{\text{kpc}} = 2.12 \left(\frac{M\,(d)}{10^{11} M_\odot}\right)^{1/2},\ \text{where } b = \frac{0.32}{Y} \tag{13}$$

I take first as a detailed example two models of our own Galaxy due to Innanen[7] (I include an extra factor of 1.5 in (12) and (13) to correct for random orientation of the Galaxy). For each model we can solve (13) and work out the effective mass of the lens as a function of z_s (Fig. 3).

Table 1 Effective Mass as a Fraction of Total Mass for Different Cosmological Models

Model (see caption to Fig. 3 for notation)	I	E	M	D&S
$M_{\text{eff}}/M_{\text{tot}}$	10%	12%	14%	22%

For the De Sitter and steady state models the effective mass increases with redshift until it equals the total mass; for the three other models the effective mass has a maximum at a particular redshift and then decreases. (This behaviour is related, of course, to the differing z-dependence of angular diameters in the respective models.) In Table 1 the effective mass is expressed as a percentage of the total mass for each cosmological model with $z_s = 1$ and averaged for the two Galaxy models.

Taking as a typical example, a source at a redshift $z = 1$ and a lens resembling our Galaxy at $z = 3/4$ in a $q_0 = 1$, $\Lambda = 0$

model, that angular diameter of the lens image, for perfect alignment is $\alpha o = 0.35''$. For magnification factors of ~ 100 to be possible the (unmagnified) angular size of the source must be $u \lesssim 0.0035''$. This corresponds to linear dimensions $\lesssim 25$ pc.

If the source, galaxy and observer are not precisely aligned ($\beta \neq 0$) then the formulae (1) which were derived for a point mass, are only slightly modified, except close to a cutoff point (Fig. 3). The cutoff occurs when the galaxy is not compact enough to act as a gravitational lens, that is, there is no non-trivial solution to (12). If the mass distribution is roughly of the form $M(r) \alpha r^2$ then a galaxy can act as a lens with a well defined focal length. This permits the possibility of magnifications far exceeding the values expected from (1). Even for more general conditions, we may substantially underestimate the magnification if we insert $M_{\rm eff}$ (given by the solution of (12) and (13) into (1)). This is because, when source and lens are aligned, the annulus is thicker than for a point mass. For a lens similar to our own Galaxy, this enhances the effective mass by a factor ~ 3.

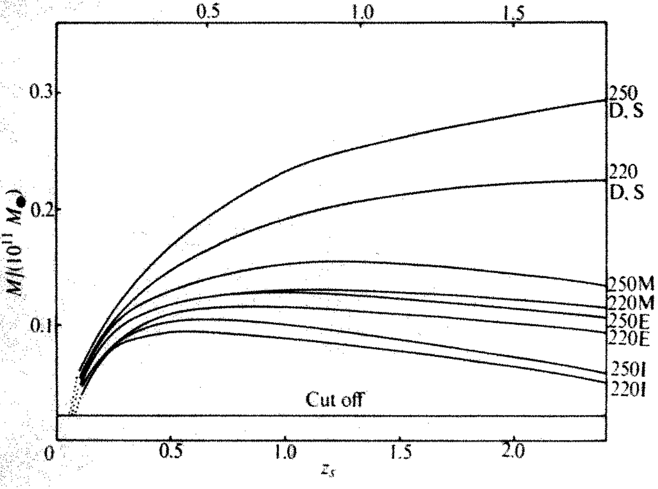

Fig. 3 The effective mass of our Galaxy as a function of redshift. Two models of our Galaxy are used with circular velocity near the Sun of 220 and 250 km s^{-1}. Five cosmological models are used: D, De Sitter; S, steady state; M, Milne,; E, Einstein de Sitter, I, $q_0 = 1$, $\Lambda = 0$ model.

Fish[8] has calculated the effective radius r_e (defined as the radius of a cylinder which includes half the projected luminosity of the galaxy) of twenty-five elliptical galaxies assuming that the galaxy obeys the law[9]

$$\text{Log}\,\frac{B}{B_e} = -\,3.33\,(\alpha_1^{1/4} - 1)$$

Where $\alpha_1 = r/r_e$, B = surface brightness, B_e = surface brightness at $r = r_e$. Assuming a constant mass to light ratio, we find that the average ratio of effective mass to total mass for ellipticals is about 30%. A similar analysis using additional data[10-13] shows that for spirals this ratio is only of order 1%. We may therefore estimate, very roughly, that the mean value of effective mass to total mass (where galaxies are weighted according to their space density and total mass) is $\sim 25\%$. De Silva[14,15] has obtained similar results, although he assumed a different form of mass distribution in the galaxies.

Luminosity Functions

A_0 is the maximum magnification of the lens when $\beta = 0$. Thus the lens images arising from magnification of sources with a given luminosity F_0 would have an apparent "cumulative luminosity function" (CLF) $Q(F) \alpha F^{-2}$ (for $\frac{F}{F_0} \lesssim 0.9 A_0$). This compares with the results $Q(F) \alpha F^{-1.19}$ and $Q(F) \alpha F^{-1.6}$ obtained by Schmidt[16,19] (Fig. 4).

If $\varphi_s(E)\,\mathrm{d}E$ is the number of sources with luminosity E to $E + \mathrm{d}E$, and $\Phi_Q(F)\,\mathrm{d}F$ is the corresponding function for lens images, then

$$\Phi_Q\,(F)\,\mathrm{d}\,F = \left(\int_x \varphi_s\,(F/x)\,\frac{p(X)}{x}\,\mathrm{d}x \right)\,\mathrm{d}\,F$$

where $p(X)$ is the probability of a source magnification being X to $X + \mathrm{d}X$.

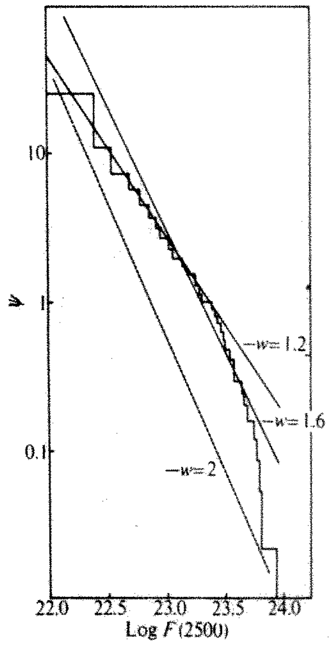

Fig. 4 The cumulative luminosity function for lens images and QSOs at a given redshift. The lens images have a logarithmic slope $-w = 2$. Shown are two curves for QSOs having logarithmic slopes at the low luminosity end of $-w = 1.2$ and 1.6.

If the CLF of the sources has a logarithmic slope flatter than $1/E^2$ then the CLF for the lens images will still be $1/F^2$. It is only if the CLF for the sources is steeper than $1/E^2$ that the lens images have the same CLF as the sources.

Number of Lens Images

The CLF of QSOs is poorly determined observationally, and a law $Q(F) \alpha F^{-2}$ is not inconsistent with the data given here. We therefore consider under what circumstances it is possible to interpret all QSOs as gravitational lens images.

As a rough estimate of the co-moving density of QSOs with log F (2,500) ≥ 22.0, at $z \simeq 2.8$, I take 1.2×10^{-5} Mpc^{-3}, which is derived from numbers quoted by Lynden-Bell and Schmidt (unpublished). They refer to QSOs above a certain threshold of radio intensity, so the estimate may be too low by an order of magnitude. In view of the great uncertainty, however, it can be adopted in the following calculations. The present density of Seyferts with $10^{20} \lesssim F \lesssim 10^{21}$ is[17] $\sim 3 \times 10^{-4}$ Mpc^{-3} and the present density of N-type galaxies with $10^{21} \lesssim F \lesssim 10^{22}$ is $\sim 3 \times 10^{-6}$ Mpc^{-3}. If we make the conservative assumption that Seyferts and N-galaxies have the same density (per co-moving volume) at all epochs, and that there are no effective lenses apart from elliptical galaxies, then we find from (7) that the number of lens images out to $Z = 2.8$ falls short of Lynden-Bell and Schmidt's estimate by a factor of $\sim 10^4$ for a $q_0 = 1$, $\Lambda = 0$

model and $\sim 2\times10^3$ for a $q_0=\frac{1}{2}$, $\Lambda=0$ model. Thus on this ultra-conservative hypothesis, it is unlikely that even one of the known QSOs can be interpreted in this way. The number of lens images would obviously be enhanced if a large amount of additional matter existed in the form of "dark objects" sufficiently compact to act as effective lenses. Even if the smoothed-out present density of such objects amounted to 4×10^{-29} g cm^{-3} (corresponding to the overall mean density of a Friedmann model with $q_0=1$), we would still only be able to account for $\sim 0.3\%$ of all QSOs as lens images. (This number is rather uncertain and may be as high as 1% or 2%. But, even if this were the case, then in order to explain all QSOs as lens images we still need evolution in the sources.)

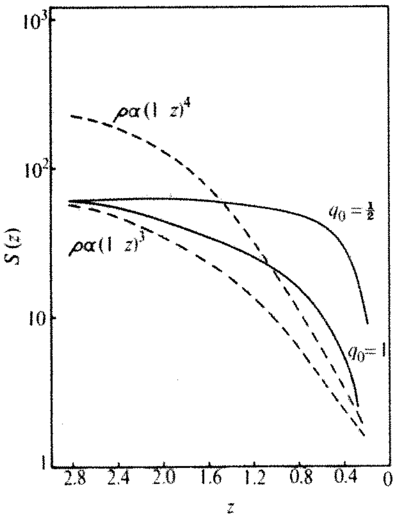

Fig. 5 Co-moving density of sources (Seyfert and N-galaxies) $S(z)$ as a function of redshift for two cosmological models assuming all QSOs are lens images. Also shown are evolution laws $\rho\alpha(1+z)^3$ and $\rho\alpha(1+z)^4$. There is a large uncertainty in the normalization of the curves.

This result can be deduced from the work of Refsdal[18], who has calculated the apparent-luminosity distribution of distant light sources in a universe where all the material is concentrated in point masses. He finds, in effect, that the CLF for the images must, at all redshifts, be below the line $\psi_L\ \alpha\ \frac{1}{F^2}$ (where F is the luminosity) extrapolated from the unmagnified luminosity function of the sources. This condition would be violated if the QSOs at large redshifts were all lens images of Seyfert and N-galaxies, and the latter had the same coordinate density as at the present epoch. Refsdal's analysis includes the more general case when the apparent luminosity is affected by several masses close to the line of sight[19–22].

The numbers quoted for the density of Seyfert, N-galaxies and QSOs are not very well determined, but in order that Refsdal's condition is not violated, there must be an evolution in the co-moving density of Seyfert and N-galaxies, by a factor S, of at least 50–300 from $z=0$ to $z=2.8$, together with at least half of the density of the universe ($q_0=1$ model) that is 2×10^{-29} g cm^{-3} in the form of dark compact objects, in order that the expected number of lens images corresponds to the number of QSOs out to a redshift $z=2.8$.

An even larger factor for the evolution of Seyfert and N-galaxies would allow a proportionally smaller smoothed out density of objects which act as lenses.

In Fig. 5 I plot, using (10), the relative co-moving density $S(Z)$ as a function of redshift for Seyferts and N-galaxies based on two cosmological models, assuming that all QSOs are lens images. The normalization is rather uncertain. Even without evolution in the sources, the lens images evolve quite rapidly (see (8)). Hence, when we introduce evolution of the sources, and assume all lens images are QSOs, we obtain a rapid increase in the density of sources from $z=0$ to $z=0.4$ together with a slow increase for $z>0.4$ which can be seen in Fig. 5.

Properties of Lens Images

If the lenses are predominantly "dark objects", and not ordinary galaxies (as must be the case if the lens effect is to be astronomically significant), then in order that the appearance of the lens images be starlike the masses of these objects cannot be too great. For $z_s=1$, $M_{\rm eff}<2\times10^{11}\,M_\odot$; and for $z_s=0.2$, $M_{\rm eff}<16\times10^{11}\,M_\odot$.

I have assumed when working out the luminosity function that $A\ll A_0$. The value of A_0 is given by $A_0=\alpha_0/u$. Assuming a constant α_0 and that the Seyfert nuclei have a standard size, then $\frac{u=H_0\,d}{z'}$ where d is the radius of the Seyfert nuclei, $z'=z'$ (z, model). For small z, $z'=z$.

Thus

$$A_0 = \frac{\alpha_0\,c\,z'}{H_0\,d}$$

So as we go out to a larger redshift A_0 increases. The line emitting region in Seyfert and N-galaxies is larger than the continuum region, thus when there is a high magnification and the source lens and observer are well lined up, the continuum region will be magnified more than the line region.

Taking an example of our Galaxy at $z=3/4$ and a source at $z=1$, if we define:

$$A_1 = \frac{2{,}500}{r_{\rm pc}}$$

where $r_{\rm pc}$ is the radius of the line emitting region, then the continuum to line ratio will be higher for lens images which result from magnifications greater than $\sim A_1$.

For $r_{\rm pc}\sim100$ pc, $A_1\sim25$, and the high luminosity tail of the lens images

$$\left(\frac{F}{F_0}\gtrsim 25\right)$$

would all have their continuum enhanced relative to their line emission.

The luminosity function for sources and lens images cannot be a continuous function but must exhibit a break between the two populations. If most QSOs are lens images then the luminosity function should show a distinct upward trend in going from QSOs to N-galaxies. There is some evidence for such a situation (D. Lynden-Bell, unpublished work). The break becomes less marked for higher redshifts.

Another difficulty in interpreting QSOs as gravitational lens images is to explain extended radio features. An extended source cannot be magnified, and any extended radio components of QSOs have to be attributed to either the lens galaxy or the source. The Seyfert galaxies in general do not show many radio features, and none of the observed ones has the double radio source structure that so many QSOs exhibit. I have, however, shown that the N-galaxies make a significant contribution as sources of gravitational lenses, and many of them do show double radio source structure.

This might provide an explanation why the radio, N-galaxies, and QSOs which exhibit double radio source structure all seem to follow a natural sequence[23].

If the lens or object has a proper motion then the amplification will change with time. Typically, however, the time scale for a change of 0.1 mag is $\sim10^3$ yr. The Earth's motion around the Sun will result in a change of only about 10^{-5} mag over the year.

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Reconstruction of the South-West Pacific Margin of Gondwanaland

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New Zealand and the surrounding regions of the South-West Pacific have undergone a complex tectonic development since the break-up of Gondwanaland began in the Mesozoic. In this article, data relevant to reassembly of the continental fragments in the South-West Pacific are examined and a fairly detailed reconstruction is proposed as a basis for further discussion.

PREVIOUS reconstructions have been made of the Australia–Antarctica fit[1-3] and, following recognition of the transcurrent nature of the Alpine Fault[4], geological interpretations of the New Zealand area have been proposed[1,5,6]. Regional reconstructions on a larger scale have also been attempted[1,7-12], but these have failed to make full use of bathymetric, geophysical, geological and tectonic relationships. In some cases[9-11] large faults and displacements have been postulated for which there is no geological evidence.

The starting point for the reconstruction presented in this article is the fit of Australia and Antarctica, which has been independently computed using the 1,000 fathom line[2] and the 500 fathom line[3]. These fits are essentially identical and require that the Australian and Antarctic plates be moved back together along lines parallel to the observed transform faults. Geological data from the Antarctic coast seem to support this reconstruction and it is unlikely to require extensive modification.

The remaining fragments of the old Gondwana continental crust have to be defined before refitting them against Australia–Antarctica. I have done this by interpretation of bathymetric maps, aided by available data on crustal thickness deduced from seismic refraction profiles and geological data. Fig. 1 is a compilation of bathymetric data and in Fig. 2 I have delineated the continental areas as discussed below and sketched the geology and the plate boundaries that are at present active.

In drawing the boundary of an area of continental crust, the relationship between crustal thickness and bathymetry is the chief consideration. When a continental block breaks apart, "necking" occurs between the fragments until, ultimately, new oceanic crust begins to form between them[13,14]. The edge of the continental block is then a transition zone from continental crust (25 to 50 km thick) to oceanic crust (5 km thick) and the boundary of the block must be drawn within this zone. In the case where the block is above sea level, this level is taken as the edge of the continental shelf using the 1,000 m line. Where the continental slope is steep, the contours are closely spaced and a reasonably precise delineation of the block is thus possible. In the case of submerged areas with relatively gentle slopes the edge of the block cannot be so closely defined.

The edge of the Australian–Antarctic block is drawn at the 1,000 m contour. The continental slope is steep except in the Coral Sea region (Fig. 1) where extensive reefs and seamounts complicate the bathymetry. Recent refraction profiles[15] have shown that the Queensland Plateau is underlain by continental crust and the 2,000 m line is used here to include it as part of the Australian block.

New Zealand is only a small part of an extensive submarine plateau (Fig. 1). To the south and east, the Campbell Plateau and Chatham Rise are underlain by continental crust[16]. Typically "continental" rocks outcrop on the islands on these plateaux and these have strong affinities to New Zealand rocks, suggesting that the plateaux are offshore extensions of New Zealand[6,8]. The 2,000 m contour is used here to delineate the edge of the New Zealand block.

Two broad submarine ridges extend north-west from New Zealand. Recent work[17] confirms earlier views[18] that both the Lord Howe Rise and Norfolk Ridge are comprised of crust of continental character. The Norfolk Ridge continues to New Caledonia, which is closely related geologically to New

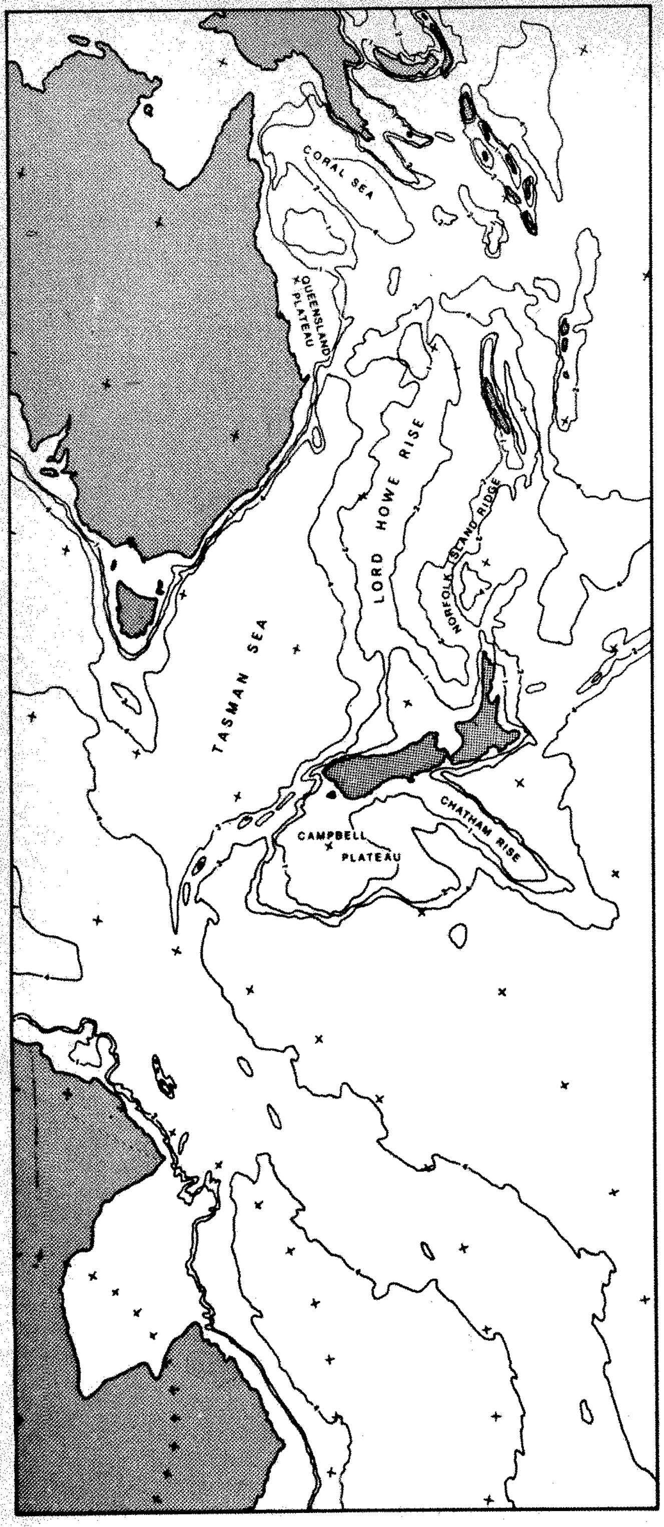

Fig. 1 Bathymetric map of the South-West Pacific, showing 1, 2 and 4 km submarine contours. (Based on a composite projection. ×, 10° intersections.)

Zealand[19]. This ridge probably represents the eastern margin of Gondwanaland before break-up, for the ridges and islands to the east are all much younger. The "edge" of the Lord Howe Rise and Norfolk Ridge is difficult to define accurately, as they both have gentle slopes, and is here taken at the 2,000 m line (Fig. 2). The Tasman Sea is underlain by oceanic crust[17,18] and the crust in the New Caledonia Basin is much thinner than on the flanking ridges[17].

The Louisiade Ridge, an offshore continuation of New Guinea, also has continental characteristics[15]. Reefs in the area complicate the bathymetry but parts of the Louisiade and Rennell Ridges are probably fragments of continental crust. The limits of this crust cannot be drawn with certainty and are only sketched in the reconstruction.

Finally, part of the Solomon Islands may be a fragment of continental crust. Officer[18] suggests a crustal thickness of 15 km and the occurrence of a probable Cretaceous igneous and metamorphic basal complex[20] indicates that part of the Solomon Islands may be a fragment of the outer edge of the Papuan Geosyncline.

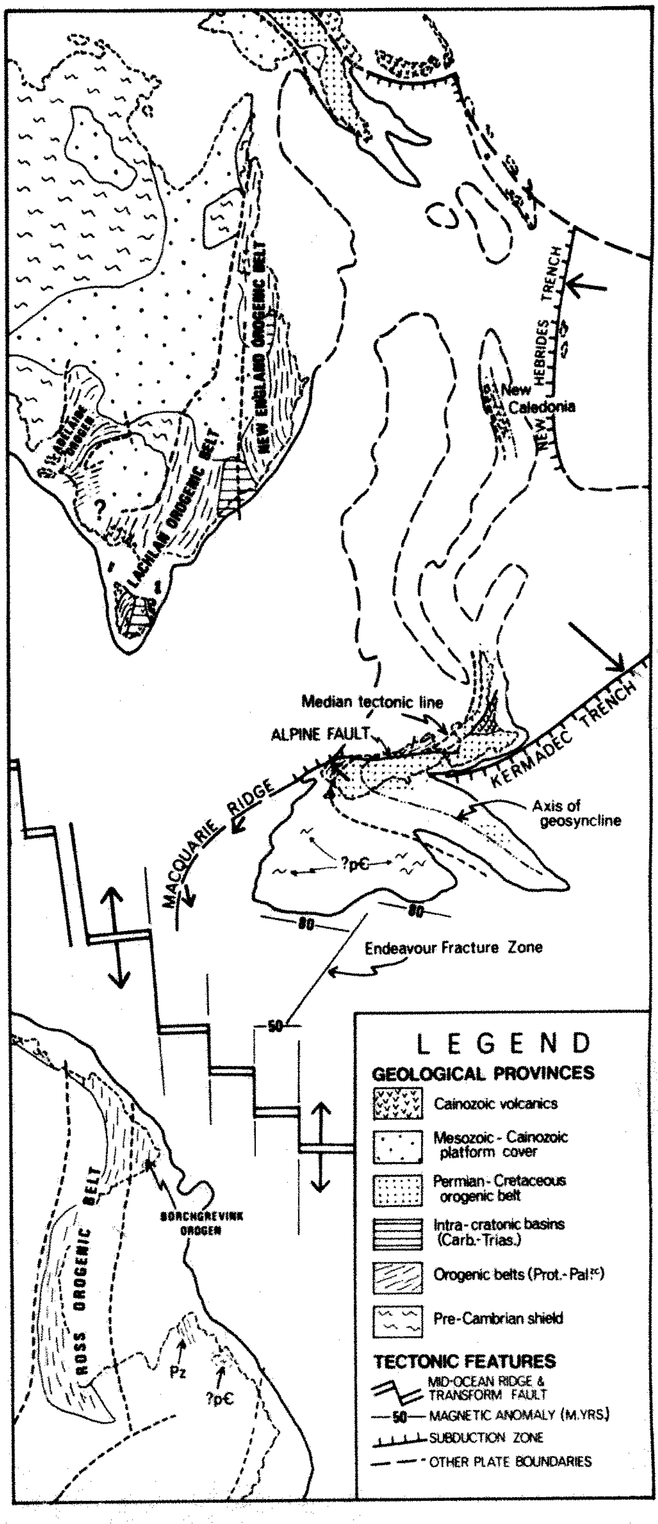

Fig. 2 Geology and recent tectonics of the South-West Pacific. Areas of continental crust are bounded by solid and dashed (where less precise) lines. (Same projection as Fig. 1.)

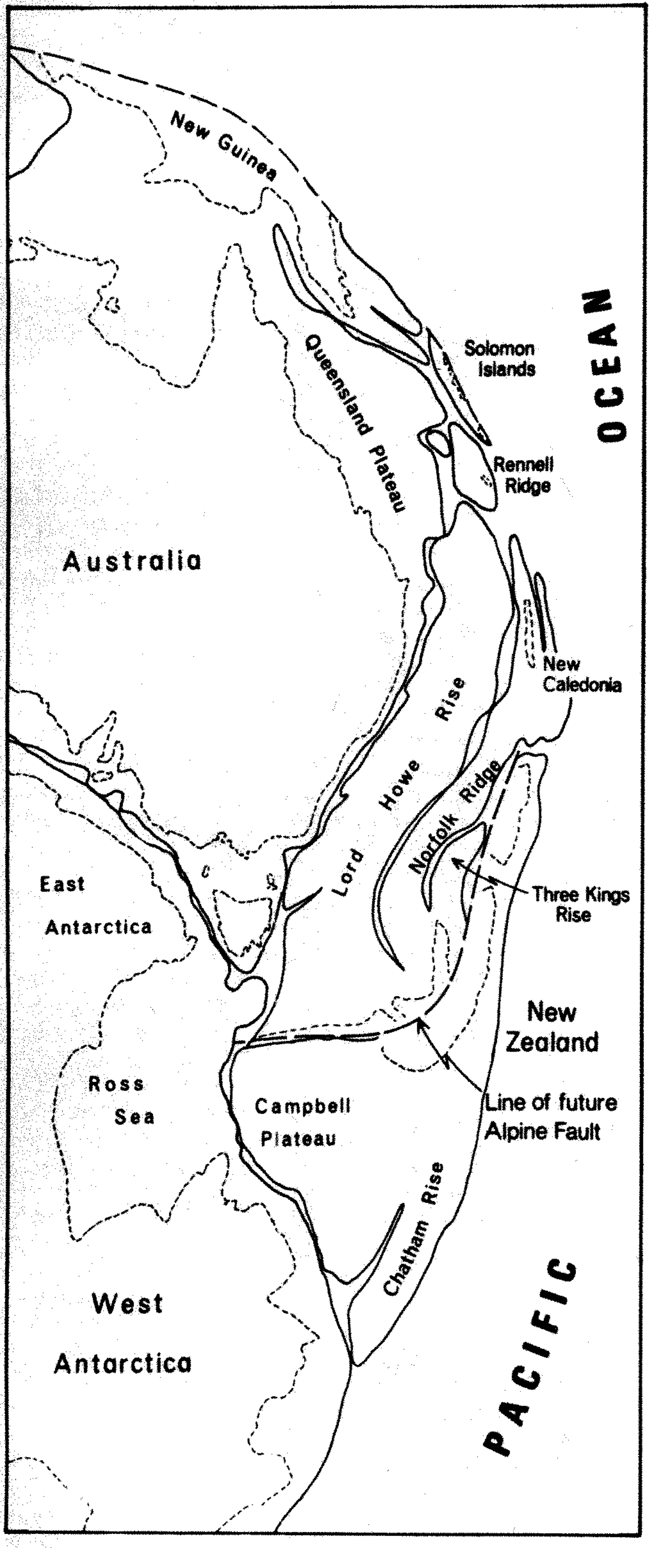

Fig. 3 Morphological reconstruction of the South-West Pacific margin of Gondwanaland. Present topographic names given for reference.

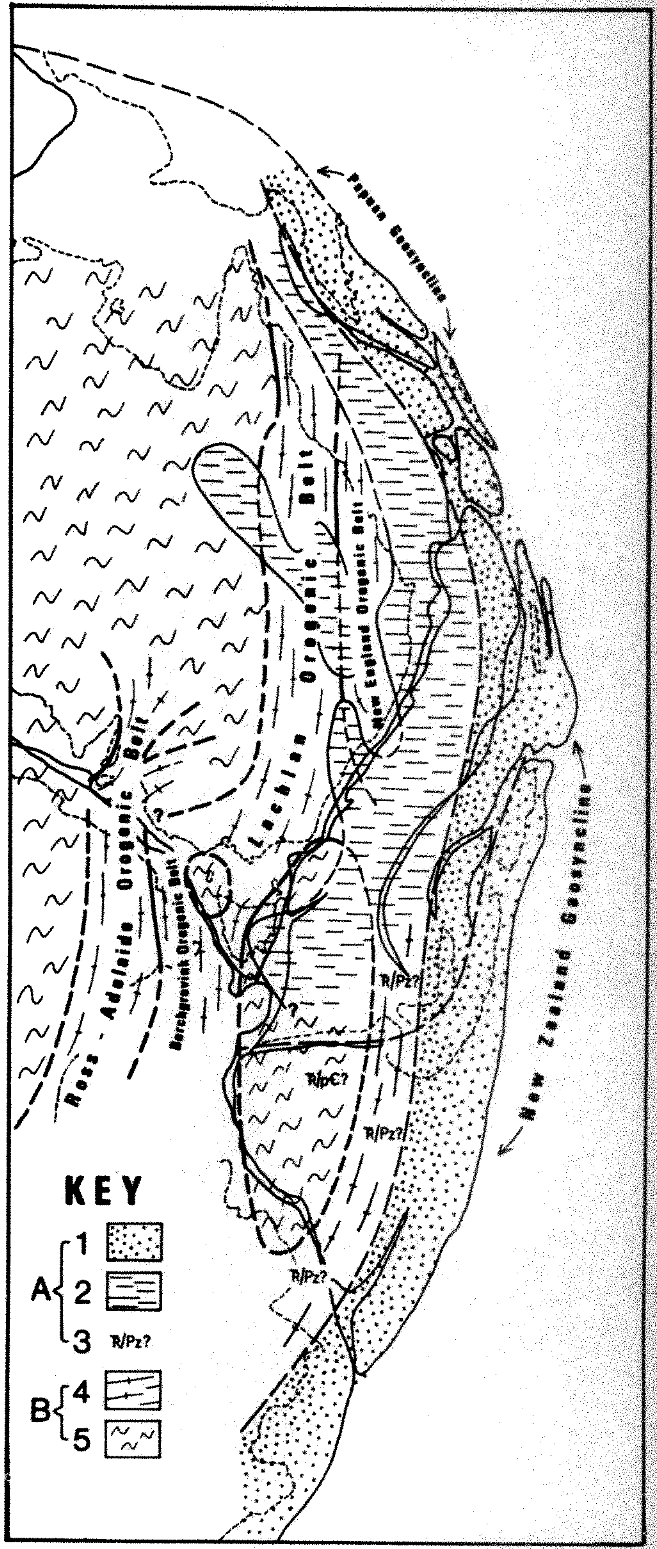

Fig. 4 Triassic palaeotectonic map superimposed on Fig. 3. *A*, Areas of Triassic deposition: 1, Geosynclinal sediments along Pacific margin; 2, platform and intracratonic basin sediments in eastern Australia; 3, inferred platform sediments on Palaeozoic (Pz) and Precambrian (pC) basement in New Zealand and Antarctica. *B*, Stabilized continental crust: 4, Late Proterozoic and Palaeozoic orogenic belts (see text); 5, Precambrian shield.

Reassembly of Fragments

The geological and tectonic features which provide a framework for the reconstruction are shown in Fig. 2 and the Australia–Antarctic fit[1-3] is the basis of the reassembly. The next stage is the closure of the Southern Ocean between New Zealand and Antarctica. Marine magnetic profiling results indicate that the Pacific–Antarctic Ridge formed between the Campbell Plateau and West Antarctica during the late Cretaceous (80 m.y. BP, ref. 21) and that a great change in spreading direction occurred in the early Eocene (50 m.y., ref. 22). Reversal of separation to 50 m.y. BP brings the Campbell Plateau and West Antarctica closer together. It has been shown that the spreading rate from 50 to 80 m.y. BP increased eastwards across the Endeavour Fracture Zone[22] and reversal of this motion leads to a relative clockwise rotation of the Campbell Plateau to bring it up against West Antarctica. The morphological fit between these blocks seems to be very good and could probably be tested by mathematical analysis. The Chatham Rise is then laid back against the Campbell Plateau, closing the Bounty Trough and completing this part of the reassembly (Fig. 3).

South of the Queensland Plateau the northern end of the Lord Howe Rise is close to the Australian block. The Tasman Sea seems to have opened as a sphenochasm[1] and there is no evidence for north–south transcurrent displacements at its northern end. The Lord Howe Rise can, therefore, be replaced directly against Australia, thus closing the Tasman Sea (Fig. 3). Precise morphological correspondence cannot be demonstrated because of the poor definition of the Lord Howe Rise.

A large displacement between the Campbell Plateau and the southern end of the Lord Howe Rise is required to close the Tasman Sea completely. This displacement is identified with the Alpine Fault of New Zealand (Fig. 3). The amount of lateral displacement required to complete the morphological fit is equal to the observed transcurrent movement on the Alpine Fault and thus, in the reconstruction, pre-drift New Zealand assumes the configuration postulated by previous workers[1,5,6]. But the only important internal deformation in any of the blocks in this reconstruction is along the Alpine Fault zone through New Zealand and the length of the Lord Howe Rise is just sufficient to fit in the available space between the Queensland and Campbell Plateaux.

The Norfolk Ridge is laid back against the Lord Howe Rise (Fig. 3), closing the New Caledonia Basin. The projection of the Alpine Fault through North Island, New Zealand[23], is used to bring the eastern part of North Island towards the Three Kings Rise, and this completes the continuity of the New Zealand Geosyncline (Fig. 4).

Finally, the Coral Sea sphenochasm is closed, thus bringing eastern New Guinea against the Queensland Plateau; the remaining continental fragments are fitted into the gap between New Guinea and New Caledonia (Fig. 3).

This reconstruction does not require new transcurrent faults to be postulated and maintains internal stability within the continental blocks; only seafloor spreading and the formation of new ocean basins are needed to achieve the present configuration.

Geological Considerations

The regional geology is summarized in Fig. 2 and three divisions can be recognized: (*a*) Precambrian basement rocks; (*b*) late Precambrian and Palaeozoic orogenic belts, and (*c*) Mesozoic and Tertiary orogenic belts.

Precambrian basement rocks form the nucleus of Australia and East Antarctica and generally comprise high-grade metamorphics, crystalline intrusives and extrusives and some areas of relatively undisturbed sediments, which together form the "foreland" to the succeeding events. The eastern part of Australia has experienced a complex sequence of events which is only understood in principle at present. Further work is in progress on the interpretation of this area (Solomon and Griffiths, unpublished results) and only the outline will be considered in this article.

In eastern Australia, two late Precambrian to Palaeozoic deformed belts are recognized—the Adelaide and Tasman Geosynclines. The continued use of the term geosyncline in this context is inappropriate (Solomon and Griffiths, unpublished results) and instead we refer to the Adelaide Orogenic Belt and the Tasman Orogenic Zone. The Tasman Orogenic Zone is further divided into two units, the Lachlan and New England Orogenic Belts. The present position of these belts is shown in Fig. 2, and their position on the reconstruction is indicated in Fig. 4.

The Adelaide Orogen in South Australia is composed of a thick Proterozoic to Cambrian sedimentary sequence, which underwent high level paratectonic[24] deformation during the Lower Ordovician. In Antarctica the Ross Orogen shows a parallel development, with Proterozoic to Cambrian sedimentation followed by late Cambrian–Ordovician deformation[25], and these two belts are aligned in the reconstruction.

The Lachlan Orogen is composed of deformed Cambrian to Devonian sediments. It is internally complex and Cambrian to Devonian orthotectonic and Ordovician to Devonian paratectonic sequences are recognized. An important orogenic event occurred in the mid-Devonian. The Lachlan Orogen continues into Antarctica as the Borchgrevink Orogen in northern Victoria Land[25], where the metamorphosed Cambrian Robertson Bay Group has an infaulted strip of Silurian (?) to Devonian Bowers Group sediments[26]. The whole orogen was intruded by granites and stabilized as continental crust by the late Devonian.

Sequences similar in age and variety of deformational style occur in North-West Nelson and Fiordland, New Zealand, where a Cambrian to Devonian orthotectonic unit and an Ordovician to Devonian paratectonic sequence are recognized (my unpublished results).

To the west of the Alpine Fault and to the south of these Lachlan sediments, probable Precambrian rocks occur[27] and I suggest that a large Precambrian block was present within the Lachlan Orogen (Fig. 4). Precambrian rocks form a basement to Lachlan sediments in Tasmania and possible Precambrian rocks occur in Marie Byrd Land, West Antarctica[25] (Fig. 2); this Precambrian block is, therefore, tentatively drawn as in Fig. 4. The rocks exposed in North-West Tasmania are considered to be part of a smaller Precambrian block (Fig. 4).

The New England Orogen is a Silurian to Permian belt which is also internally complex; its outcrop is confined to eastern Australia at present (Fig. 4). The last stages of granite intrusion in the New England Orogen, in the Permian, completed the stabilization of the Palaeozoic margin of Gondwanaland as continental crust. Thereafter until the mid-Jurassic sedimentation continued along the Pacific margin, forming the Papuan and New Zealand Geosynclines (Fig. 4). This geosynclinal belt underwent orogenesis from mid-Jurassic to mid-Cretaceous; the continent then began to break apart; the fragments attained their present configuration during the Tertiary as seafloor spreading occurred (Griffiths and Varne, in preparation).

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Cholinergic Receptor Molecules and Cholinesterase Molecules at Mouse Skeletal Muscle Junctions

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Studies of the binding of labelled α-bungarotoxin to mouse skeletal muscle endplates have allowed the quantification of acetylcholine receptor sites at the post-synaptic membrane.

THE molecules of acetylcholinesterase (AChE) at individual motor endplates in various vertebrate skeletal muscles have been enumerated[1,2], and in mouse muscle endplates[3,4] they have been located principally or entirely at the post-synaptic membrane. The methods used[1,2,5] rely on reaction of AChE with radioactive diiso-propylfluorophosphate (DFP) (with appropriate chemical devices for specificity) and cellular autoradiography. We report here the next step in the analysis of functional components at the motor endplate, that is, the counting *in situ* of the molecules of the cholinergic receptor.

For this purpose, an agent is required that binds irreversibly and with high specificity to the cholinergic receptor. There is extensive evidence[6-9] that α-bungarotoxin, isolated from the venom of the snake *Bungarus multicinctus*, has the desired properties. We have, therefore, labelled α-bungarotoxin with tritium to high specific activity, for reaction at mammalian motor endplates and quantitative autoradiography.

Labelling of Receptors

B. multicinctus venom was fractionated[10] on 'CM-Sephadex C-50': the α-bungarotoxin was eluted in the second of the nine protein peaks separated. Two chromatographic separations on CM-cellulose (Whatman CM-52) in 0.05 M ammonium acetate (pH 5.8) yielded a peak of pure α-bungarotoxin. Labelling was by reaction[11] with ^{3}H-acetic anhydride, with isolation by two gel filtrations on 'G-25'. The product (^{3}H-α-bungarotoxin) contained radioactivity corresponding, in three preparations, to 0.40 to 0.80 acetyl groups per toxin molecule, and had an LD_{50} in mice and a blocking potency on the rat phrenic-diaphragm preparation[6] equal to those of the pure unlabelled toxin.

After lethal injection of ^{3}H-α-bungarotoxin into mice, autoradiographs prepared[1] from striated muscle sections showed a clear cut and specific labelling of all endplates (Fig. 1). To

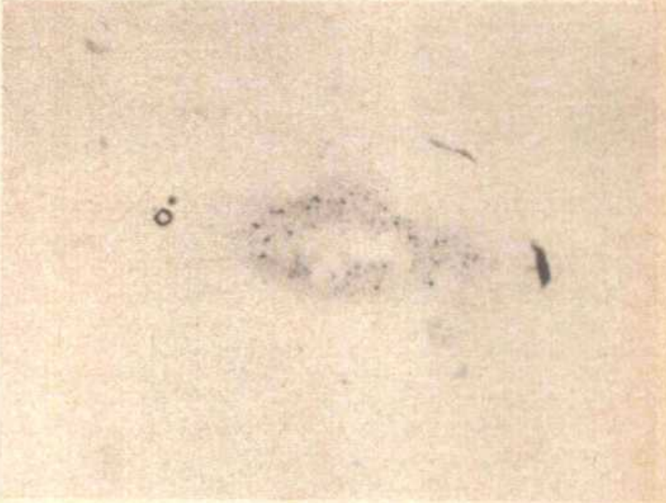

Fig. 1 Autoradiograph (18 days exposure) of diaphragm labelled with ^{3}H-α-bungarotoxin, showing a single endplate (seen by light staining[12] for AChE, performed through the developed stripping film). Note that outside the endplate area, labelling is at background level only.

phrenic nerve-diaphragm preparations from male mice (17–20 g), ^{3}H-α-bungarotoxin (10 μg ml.$^{-1}$) was applied in gassed Tyrode solution at 37° C, with recording of isometric twitch tension on a Grass 5D polygraph. The twitch and tetanic responses both declined to zero over about 12 min (Fig. 2, curve *a*). After various reaction times, 10^{-5} M *d*-tubocurarine washes were given, followed by Tyrode washes and autoradiography[1]. Such *d*-tubocurarine treatment was shown to protect effectively from the ^{3}H-α-bungarotoxin reaction, confirming the evidence[6,7,9] for the specificity. Repeated washes of portions of a labelled muscle with Tyrode did not reduce the final mean grain density, confirming irreversibility. A saturating value for the mean grain density at the endplates was reached after 20–30 min total reaction, that is, later than the disappearance of response (Fig. 2, curve *b*). This maximum uptake value was shown to be the same as that reached after paralysis *in vivo* by excess ^{3}H-α-bungarotoxin (Table 1).

Table 1 Grain Densities over Toxin-labelled and DFP-labelled Endplates

Animal	Muscle	Mean grains ± s.e. per field Toxin label	 DFP label	Ratio of sites Toxin: DFP	Receptors per endplate *
Mouse 1	Diaphragm (D)	11.9 ± 0.3 (208)	26.6 ± 0.5 (184)	1.14	
2	Diaphragm	11.8 ± 0.3 (164)	33.8 ± 0.5 (170)	0.89	
3	Diaphragm	10.0 ± 0.3 (155)	14.0 ± 0.4 (190)	1.00	
4	Diaphragm	14.1 ± 0.2 (274)	21.0 ± 0.4 (186)	1.13	
5, 6	Diaphragm	14.3 ± 0.4 (109) 13.9 ± 0.3 (109)	22.2 ± 0.4 (163)	1.09	
5, 6	Sternomastoid (S)	15.7 ± 0.4 (145) 15.6 ± 0.4 (145)	28.9 ± 0.4 (148)	0.92	
Mouse (mean)				1.02	(D) 3.0 × 10^{7}
					(S) 8.7 × 10^{7}
Chicken 1	Post. latiss. dorsi	11.8 ± 0.3 (160)	16.0 ± 0.2 (251)	1.01	3–5 × 10^{7}
2	Biventer	11.6 ± 0.4 (86)	14.6 ± 0.4 (165)	1.09	

Labelling was *in vitro*, with ^{3}H-α-bungarotoxin at 10 μg ml.$^{-1}$, 37° C, 45 min; except that mouse 5 was killed by a five-fold supra-lethal dose of ^{3}H-α-bungarotoxin and its muscles were autoradiographed with (upper line) or without (lower line) a further exposure to ^{3}H-α-bungarotoxin *in vitro*. The ^{3}H-DFP labelling, in that case only, was performed on muscles from another animal (6), autoradiographed on the same slides. Specific activity (Ci mmol^{-1}) of ^{3}H-DFP was 3.24, and of ^{3}H-α-bungarotoxin preparations was from 1.26 to 2.32. Number of labelled endplate fields (6 μm × 6 μm) shown in parentheses. Chicken data obtained by Dr J. Jedrzejczyk.

* Number of α-bungarotoxin binding sites per endplate, taken (since the ratio is 1.0) as the absolute number of the DFP-reactive sites per endplate, measured[1,2] by β-track counting of micro-dissected fibres from ^{32}P-DFP-labelled muscles, from four to six animals in each case. For chicken muscles, range arises from different ages and hence fibre sizes.

Structures which were well labelled with ^{3}H-α-bungarotoxin but showed no staining[12] for ChE in our (minimal) conditions of incubation were occasionally encountered and were tentatively identified as motor spindles. These were not included in the counts reported, but they suggest that the receptors are not necessarily associated with AChE sites.

Comparison with Cholinesterase Molecules

At saturation, the mean density of ^{3}H-α-bungarotoxin labelled sites at the endplates was compared with the mean density of endplate sites labelled to saturation[1,2] with ^{3}H-DFP in parallel preparations from the same muscles (Table 1), yielding (with the specific radioactivities used) the ratio of these two types of site at the endplate. The endplate sites that react rapidly with DFP include AChE[1,2], but in addition comprise other cholinesterases[2,13,14]. We have now found by the autoradiographic method that 95% or more of the DFP-reactive sites at the endplates measured could be protected from ^{3}H-DFP (10^{-5} M, 22°, 30 min) reaction by the presence of 10^{-5} M eserine. We therefore take the total ^{3}H-DFP labelling at endplates (Table 1) as representing essentially the cholinesterase active centres (ChE) of all types (including AChE). Hence, the absolute number of α-bungarotoxin binding receptor sites at each endplate (Table 1) was equal to the number of ChE active centres in these two mouse muscles. Evidence that this equality may be general was obtained by using muscles from a remotely related species, the chicken (Table 1), and by approximately similar results in single experiments on rat sternomastoid and rhesus monkey diaphragm. In eel electric tissue isolated membranes, the same equality of the sites has been deduced[9,15].

The number of labelled toxin-binding sites per endplate was not changed by pre-treatment with DFP to saturation of the ChE sites, nor did saturation with the toxin decrease the ^{3}H-DFP labelling. Hence the two types of active centres at the endplate are distinct and independent.

Waser and co-workers[16,17] have estimated the cholinergic receptor active centres in the mouse diaphragm endplate to be about eight times less than our value. The ^{14}C-labelled curariform drugs they used bind reversibly and are readily washed out, and autoradiographs at the single endplate level were not obtained in that method[16,17]; we believe that these factors led to an underestimate of the total of cholinergic receptor sites at this synapse.

Molecular Requirements for Transmission

The time-course of the inhibition of transmission (Fig. 2, curve *a*) was distinctly different from the time-course of the binding of the toxin seen at the endplates. A curve relating receptor occupancy to response blockade was constructed thus, and was confirmed by measurements of the uptake at endplates made by autoradiography of some individual recorded preparations (Fig. 3). The results of Fig. 3 agree qualitatively with those obtained[18] less directly by a dose-ratio analysis of effects of reversible antagonists and stimulants on two cat muscles. By our method, all the fibres still responded when, on the average, 45% of the receptor sites were blocked. The steep rise in inhibition is centred at 70% receptor blockade and this mid-point is attributed to the depression of the endplate potential to the threshold of the muscle action potential in the average of the population of fibres. That threshold is close to 35 mV above the resting potential, while the total range of depolarization that release of transmitter can produce at the unblocked endplate is about 75 mV above the resting potential[19,20]. The data suggest, therefore, that if there are spare receptors, that is, receptors that can be irreversibly blocked without decreasing the maximum (75 mV) depolarizing effect of the normally released transmitter, these must be less than one-half of the total present. Definition of the precise course of the response as the receptors become occupied will be possible by a combination of the autoradiographic technique with intracellular electrical recording methods. Already, however, the data of Figs. 2 and 3 exclude the case that there is a substantial reserve of receptors at the endplate.

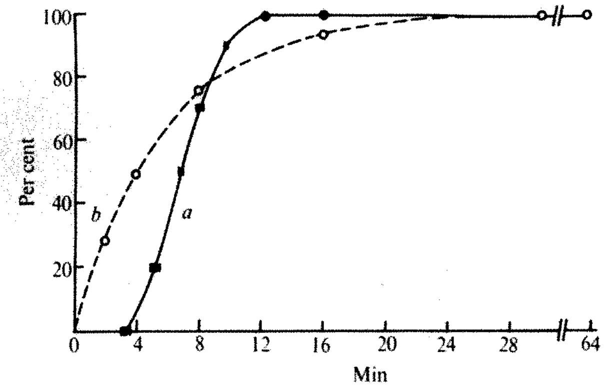

Fig. 2 Reaction of diaphragm endplate *in vitro* with ^{3}H-α-bungarotoxin (10 µg ml.$^{-1}$, 37° C). *a*, Inhibition (%) of twitch or tetanic (120 stimuli s^{-1}) response. Mean ± s.d. of the preparations from ten mice shown (s.d. omitted for values at 100%). *b*, Endplate labelling (each point is the mean for 100–200 fields over endplates), expressed as a percentage of the maximum. Preparations from two mice each gave the same curve.

By precisely similar methods, we have followed (ref. 21 and E. A. B. and J. W., in preparation) the effect on the muscle response of the progressive occupation by DFP of the ChE active centres. The requirement for the ChE (or the AChE) molecules for transmission is less stringent. Twitch potentiation commences when 65% of the ChE sites are inhibited, but the single twitch response persists when all of the ChE sites are blocked with DFP. Tetani evoked at 60 impulses s^{-1} were sustained when not more than 5% of the AChE sites were free. For higher frequencies of transmission, on the other hand, appreciable amounts of the enzyme are required to remove excess acetylcholine; for example, the tetanic response at 120 s^{-1} required about 20% of the ChE sites to be unblocked.

From our results we draw the following conclusions. (1) At several types of endplates, the number of cholinergic receptor sites is equal to the number of ChE active centres. This is not due to an identity of the two types of active centre. (2) If the receptor molecules, as well as the ChE molecules, are on the post-synaptic membrane, they are at a density of about 12,000 µm^{-2} of membrane, which is the density found[3,4] for the ^{3}H-DFP-reactive sites in two mouse muscle types. It is interesting that, using different methods, the same value (roughly 10,000 µm^{-2} of post-synaptic membrane) was deduced recently[15] for the α-bungarotoxin binding sites in a preparation from *Torpedo* electroplaques. (3) Not more than 6×10^{6} molecules of acetylcholine are released per impulse at 37° C at the rat diaphragm endplate[22,23]; taking the known number of DFP-reactive sites at this endplate[2] and the equality noted above, there are, therefore, about five cholinergic receptor sites per transmitter molecule available for single impulse transmission. Even so, there is no substantial reserve of functionally spare receptors. (4) The ChE and receptor numbers together correspond (if all are in the post-synaptic membrane) to a high density, about one subunit per 5000 Å^{2}. The simplest model compatible with all the data involves a mosaic of receptors and ChE over the whole post-synaptic membrane.

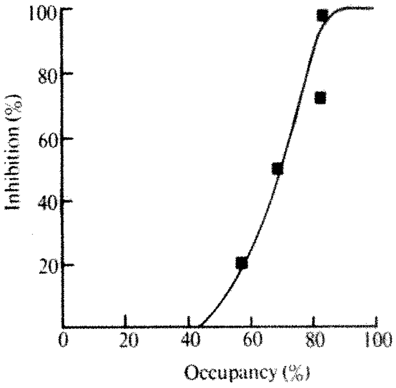

Fig. 3 Curve relating the percentage inhibition of response to the percentage of the ^{3}H-α-bungarotoxin-binding sites occupied. The curve was constructed from the two curves drawn in Fig. 2. The squares represent four additional experiments, in which the labelling of a preparation in the same conditions was arrested when a given value of the response inhibition was reached. The arrest was by removal to, and repeated washing in, *d*-tubocurarine (5×10^{-5} M) solutions in Tyrode. The second half of the same diaphragm in each case was labelled simultaneously to saturation, and both tissues were autoradiographed, so that the percentage occupancy of the toxin-binding sites could be directly determined.

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LETTERS TO NATURE

PHYSICAL SCIENCES

80 MHz Observations of the Scorpius X-1 Source

Andrew and Purton[1] discovered a weak high frequency radio source, which they identified with the strong X-ray source Sco X-1. The identification was confirmed by Ables[2], who also discovered significant changes in the source's flux density. A subsequent high resolution study of the region by Hjellming and Wade[3] at 2,695 and 8,085 MHz showed clearly the presence of three closely spaced sources; the central source was found to be highly variable over a period of hours and was identified with the optical object associated with the X-ray source. It was noted that its flare emission tended to be considerably stronger at 2,695 MHz than at 8,085 MHz, with spectral indices of up to 1.5.

Unsuccessful efforts have been made to detect the Sco X-1 source at lower frequencies by Apparao[4] (327 MHz) and Jauncey[5] (408 MHz). In Jauncey's observation the region could be observed for a total time of only about 1 min. This was adequate for setting an upper limit to the intensity of the outer non-variable sources, but the chances of observing flare activity on the variable source were slight. Apparao's observations covered a total of 10 h distributed over five nights, but his sensitivity was sufficient to detect only a strong flare of ~ 0.05 flux units at 2,695 MHz with a spectral index of 1.5 continued to 327 MHz.

During four nights in May and July 1971 the 80 MHz radioheliograph operated by the Division of Radiophysics, CSIRO, at Culgoora, NSW, was used to observe the Sco X-1 region for a total of 14 h. The observations were made by straddling the declination of the X-ray source with eight $3'.7 \times 3'.7$ beams spaced $2'.1$ apart in declination. The region was permitted to drift through the beams, which were repeatedly placed ahead of the source in a 64 s cycle; the scans surveyed an area of $15' \times 16'$ arc centred on Sco X-1. The outputs corresponding to the eight beams were recorded digitally and hour-long blocks of scans were later averaged.

We failed to detect a source in the region in any of the 14 hour long averages. The r.m.s. fluctuation in each averaged scan was ~ 0.25 f.u.; with a detection criterion of 6 × r.m.s. fluctuation the upper limit to the flux density of Sco X-1 averaged over any 1 h (the duration of a typical centimetric radio flare) was 1.5 f.u. Although the two non-variable sources of Sco X-1 lie within one radioheliograph beamwidth of the central source, they would not have been detected with this sensitivity. But even one of Hjellming and Wade's weaker flares of 0.02 f.u. at 2,695 MHz would have been visible if a spectral index of ≥ 1.2 had continued to 80 MHz.

These observations combined with those of Apparao represent a total low frequency observing time of 24 h distributed over nine nights. Hjellming and Wade's observations indicate that several radio flares would be expected to occur in that time. We therefore conclude that the high spectral indices noted by them are not continued into the low frequency end of the spectrum.

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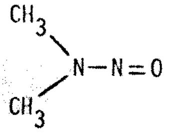
Organic Analyses of Selected Areas of Surveyor III recovered on the Apollo 12 Mission

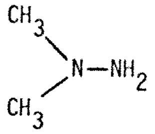
THE Apollo 12 astronauts recovered the television camera, the trenching scoop and a few smaller items from Surveyor III, which had been on the Moon for 31 months[1]. They noticed that the white surfaces of the spacecraft had become tan. The television camera remained in the Lunar Receiving Laboratory (LRL) during quarantine period and afterwards preliminary microscopic visual examinations and extensive photography were conducted at the LRL. The camera was then shipped to Hughes Aircraft Company for detailed studies and disassembly. Whenever possible the camera was handled and examined in laminar flow clean areas. On close examination, optical interference patterns were found on the camera mirror. The effects of lunar particles on this mirror had been observed earlier[2]. We report here the organic contamination of the mirror surface and camera exterior (shroud) attributable to the spacecraft outgassing, Lunar Module (LM) descent engine blasting, possible Surveyor III engine exhaust products —although thought to be unlikely due to the spatial configuration of the spacecraft components—and unknown sources. A more detailed report of these data will be published by NASA[3].

The camera mirror and middle shroud were extracted for organic material by washing the surface with benzene or benzene and methanol (3 : 1) squirted on by a syringe and collected in a beaker. The area of the mirror which was washed with benzene was approximately 35 cm^2. The whole operation was carried out in a class 100 organic clean room. These wash solvents (redistilled nanograde purity), as well as the sample washes, were concentrated on a rotary evaporator and the total residues subjected to high resolution mass spectrometry. The mass spectrometer system consisted of a modified GEC–AEI MS-902 high resolution mass spectrometer on-line to an XDS Sigma 7 computer[4–6].

The solvent background (less than 0.1 p.p.b.) consisted of hydrocarbons, chiefly the series C_nH_{2n-6} for $n=6$ to 16, and indications of carboxylic acid fragments, $C_nH_{2n-1}O_2$ for $n=3$ to 7, and phthalates (small peak of composition $C_8H_5O_3$). The residue from the mirror wash amounted to approximately 80 µg (about 2 µg/cm^2). It consisted principally of dioctyl phthalate, hydrocarbons of the series C_nH_{2n+2} for $n=3$ to 15, C_nH_{2n} for $n=3$ to 14, C_nH_{2n-2} to C_nH_{2n-10} for $n=5$ to 12 approximately, carboxylic acids of the series $C_nH_{2n}O_2$ for $n=1$ to 16 and 18 (palmitic and stearic acids were the major homologues of the series) and in minor amounts silicones and LM engine exhaust products. The silicone oil was substantiated by ions of compositions C_3H_9Si, $C_5H_{15}OSi_2$ and $C_7H_{21}O_2Si_3$, derived from straight chain silicones and ions of compositions $C_4H_{13}O_3Si_3$ and $C_5H_{15}O_3Si_3$, derived from cyclic silicones. The peaks attributable to LM exhaust[7,8] are NH_3, HCN, fragments CH_3NH and CH_3NCH_3, NO, and $C_2H_6N_2O$ (I).



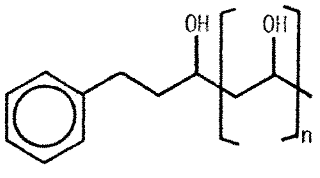
I



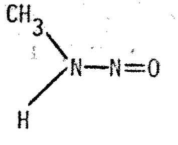
II

The nitric oxide is the major reduction product from the LM oxidizer, N_2O_4. The dimethyl oxazine (I) is a partial oxidation product of unsymmetrical dimethylhydrazine (II), the LM fuel.

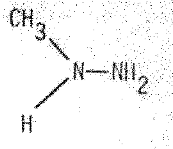
The middle shroud was washed with benzene and methanol on the side toward the LM and on the side away from the LM, and the extract residues amounted to approximately 120 µg (about 5 µg/cm^2) for the sample toward the LM and approximately 200 µg (about 8.5 µg/cm^2) for the sample leeward the LM. The major constituents found for both of these samples are hydrocarbons of the series C_nH_{2n+2} for $n=2$ to 29, C_nH_{2n} for $n=2$ to 19, C_nH_{2n-2} for $n=2$ to 16, with minor amounts of C_nH_{2n-4} to C_nH_{2n-10} for approximately $n=6$ to 13, dioctyl phthalate and silicone oil. This was substantiated by the same peaks in the high resolution mass spectral data as for the mirror sample. The minor components of these samples are nitrogenous and oxygenated compounds. A group of oxygenated peaks indicate a partially depolymerized vinyl alcohol–styrene copolymer (III)[8]. The peaks of compositions $C_{13}H_{19}O_3$, $C_{11}H_{15}O_2$, $C_9H_{11}O$, and C_7H_7 (tropylium ion) fit the pyrolytic fragmentation pattern for the copolymer III. The LM descent engine products are more varied in these samples than in those from the mirror wash, but still minor. Ions fitting the compositions NH_3, HCN, probably acetonitrile and propionitrile[7,8], NO, CH_2NO, CH_3NO, C_2H_5NO (N-hydroxyaziridine[8]) and the fragment series $C_nH_{2n}NO$ for $n=3$ to 5 and $C_nH_{2n-2}NO$ for $n=5$ and 6 are found. The peaks of composition $C_2H_6N_2O$ (I), CH_4N_2O (IV), and CH_5N_2O (a protonated species of IV) are present in significant amounts. The methyl oxazine (IV) may possibly be derived from the Surveyor III engine exhaust, because the fuel used was mainly monomethylhydrazine (V).



III



IV



V

In summary, essentially the whole outside surface of the Surveyor III television camera was covered by lunar fines, probably from the following sources: Surveyor landing, lunar transport due to meteoroidal impacts, LM landing, and redistribution during return and subsequent handling. Thus the evidence for LM and possibly Surveyor III descent engine exhaust products on the shroud and mirror is not surprising. The side toward the LM was heavily sandblasted and more discoloured than the side opposite. This fact was not too well demonstrated by the organic material isolated from the shroud, except that the total ion current for the leeward sample was about double that of the sample from the side facing the LM. The same types of organic molecules were found on the mirror and both shroud samples. The sources of the various organic contaminants[9] are as follows: hydrocarbons from lubricating oils; general terrestrial contamination from exposure and bagging material; dioctyl phthalate from polyethylene bagging material (the plasticizer); carboxylic acids from decomposition of grease and general terrestrial contamination and handling; silicones from sources as lubricating oil, outgassing of electronics and plasticizer; styrene–vinyl alcohol copolymer probably from electronics insulation; and nitrogenous compounds from LM and possibly Surveyor III engine exhaust. The organic contamination levels do not seem to contribute to the discoloration of the various surfaces.

In spite of the significant amounts of terrestrial contaminants, adsorbed mainly from exposure during examination and exhibition, as well as from the bagging materials, it was still possible to detect compounds derived from landing engine exhausts, and some compounds which may be spacecraft outgassing products. Unfortunately the LM exhaust products contaminated sample scheduled for collection by the Apollo 14 mission was not accomplished. It is rescheduled for Apollo 15. Such data will be of value in interpreting the findings of soft-landed spacecraft on other planets (for example, Viking on Mars). Furthermore, analyses for organic contaminants and identification of their sources, even if low in concentration, should be recognized as an important criterion for the design of optical or other active instruments for future spacecraft.

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Isenthalpic Flow, Joule–Kelvin Coefficients and Mantle Convection

WALDBAUM[1] has suggested that, when mantle material convects according to the model of Turcotte and Oxburgh[2], the temperature of an isolated rising mass will increase, "even in the idealized case where friction, viscosity and turbulence are ignored". He argues from the premise that the steady adiabatic flow of a fluid is isenthalpic along streamlines: the Joule–Kelvin coefficient of the fluid can therefore be used to predict the temperature change during decompression.

This argument is incorrect. Waldbaum has apparently been misled by variations in the published definitions of enthalpy. Although the enthalpy of a substance is always defined by an expression of the form

$$h = u + pv \tag{1}$$

(h = specific enthalpy, u = specific internal energy, p = pressure and v = specific volume), there are important variations in the definition of the internal energy u. Of the two authorities quoted by Waldbaum, Pippard[3] includes in h and u terms for kinetic and potential (gravitational) energy, whereas Liepmann and Roshko[4] include a term for kinetic energy in what they call "total enthalpy", but make no mention of potential energy. For them and for Landau and Lifshitz[5], however, the unqualified term enthalpy is taken to describe an intrinsic property of a substance, dependent only on local thermodynamic variables; it is "the enthalpy which would be measured by an 'observer' moving with the fluid"[4]. Pippard's definition permits him legitimately to say that, in steady adiabatic flow, the enthalpy of a fluid is constant along streamlines. For Landau and Lifshitz, however, the quantity which is constant is the sum

$$\text{enthalpy} + \text{potential energy} + \text{kinetic energy} \tag{2}$$

It can now be seen why the Joule–Kelvin coefficient $(\partial T/\partial p)_h$ is not directly applicable to free convection in a gravitational field. This coefficient is defined physically for a condition of constant intrinsic enthalpy, which does not exist where decompression occurs through upward movement in a gravitational field. For a slowly moving frictionless fluid, the stress field in those circumstances must be purely hydrostatic, and in adiabatic flow the entropy (s) will be constant. Differentiating (1) and (2) gives

$$\mathrm{d}u + p\,\mathrm{d}v + v\,\mathrm{d}p + g\,\mathrm{d}z = 0 \tag{3}$$

where g is gravitational acceleration and z is vertical height. As $v\mathrm{d}p = -g\mathrm{d}z$ in hydrostatic conditions, we obtain the standard equation of energy balance for reversible adiabatic expansion

$$(\mathrm{d}u + p\,\mathrm{d}v)_s = 0 \tag{4}$$

The temperature gradient is therefore the well known adiabatic gradient of geophysical fluid dynamics, based on the isentropic coefficient $(\partial T/\partial p)_s$.

It might be suggested that isenthalpic heating or cooling coefficients could be applied to deviations of the stress field in a real fluid from a vertical hydrostatic gradient. Such deviations could be considered to correspond to the irreversible "isenthalpic steps" of Walbaum's argument. But how large are they? The topography of the mid-ocean rift suggests ~0.6 kbar near the surface, whereas Mackenzie[6] obtained values less than 1 kbar at depths of 50 to 100 km under trenches from an analysis of gravity anomalies. Waldbaum's isenthalpic coefficients therefore suggest temperature rises of ~20 K or less. It is also questionable whether the flow is truly adiabatic in the regions of maximum non-hydrostatic stress; as Tozer[7] points out, when viscosity of a fluid varies rapidly with temperature, shear flow and associated viscous dissipation will tend to be strongly localized. The evidence of high heat flow behind island arcs tends to support this view[8]. Thus it seems likely that Joule–Kelvin coefficients will be of limited value in estimating temperature changes related to slow planetary convection.

Because of these problems it seemed worthwhile to examine further the variations in usage of the concept of internal energy among thermodynamicists. Many workers bypass the problem by not mentioning gravitational and kinetic energy at all. Gibbs[9] clearly separated gravitational energy from what he called the "intrinsic potential" of a chemical component of a thermodynamic system: he included kinetic energy[10], only to show that it must vanish at thermodynamic equilibrium. Guggenheim[11] treats gravitational energy in the same way as Gibbs, but Lewis and Randall[12] take the alternative approach and include it in the internal energy. It is unfortunate that few authors except Lewis and Randall[12] and Denbigh[13] point out the existing divergences, for there is evidently little prospect of reaching a consensus on this matter in the context of chemical thermodynamics. Considering the thermodynamics of fluid flow (a subject not usually discussed by chemical thermodynamicists) there is much to be said, however, for general adoption of the Landau–Lifshitz approach, because the kinetic and gravitational components of the total energy may often be analysed more or less independently of local thermodynamic parameters. In the absence of uniformity, confusion may be minimized by use of the adjectives "intrinsic" or "total" to indicate the sense in which the terms energy, enthalpy or chemical potential are being used in a particular context.

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Spontaneous Fission Previously Observed in a Mercury Source

PREVIOUSLY[1], we have presented evidence for the possible existence of a superheavy element with atomic number 112. The principal evidence for the possible existence of this element was based on the observation of spontaneous fission in a mercury source separated from a tungsten target which had been irradiated by 24 GeV protons. Spontaneous fission activity was observed, using polycarbonate foils, in mercury sources separated from two tungsten targets. These latter are identified by the symbols W2 and W3. In the case of the W3 source the proton dose was probably less than for W2 and also only about 30% of the mercury added as carrier was recovered in the final source (as measured by colorimetric techniques). The observed fission activity was smaller than that observed with the W2 source. In the latter case (W2) the measured activity was originally about three fissions/day and all experimental work reported here has been carried out with this sample.

The argument that the observed activity might be due to a superheavy element was based entirely on the prediction that element 112 will be the chemical homologue of mercury.

Such an identification may, of course, be in error because of the possibility of contamination of the sources. This topic was considered in some detail in our earlier work. In particular it was shown that the most likely spontaneously fissioning contaminant, ^{252}Cf (2.5 yr), could probably be excluded as there was no evidence for an associated alpha group (branching ratio 97%) at 6.1 MeV. Such a group would be expected to be sixteen times more intense than the observed rate of fission. In the case of the W3 target, immediately after the original chemical separation the Hg fraction gave 2.5 ± 0.6 fissions per week and the combined actinide-rare earth fraction gave 7 ± 2.5 fissions per week. Subsequent counting of X-rays in the Hg source indicated that less than 0.1% of all rare earths and actinides were present in the Hg fraction.

Since the earlier experiments, attempts have been made to identify the source of the observed fission activity more directly by trying to measure nuclear properties which depend in some way on the Z or A of the fissioning nucleus. As will be shown, this attempt has only been partially successful and the present letter is in the nature of a progress report on some continuing experiments, the results of which are of general interest.

With the aim of being able to measure the energy spectrum of the fission fragments some attempts were made to reduce the thickness of the W2 source and to make it more uniform. For these reasons the source was ozonized and mechanically spread on the Pt backing plate. While the source was still too thick to permit accurate measurement of the fission fragment energy spectrum, it was possible both to detect the fission fragments and measure the alpha particle energy spectrum simultaneously in the same silicon surface barrier detector. With this system we measured an upper limit of 5 : 1 for the ratio α/f, of all alpha particles having energies near 6.1 MeV to spontaneous fission activity. This indicated that at that time at most 30% of the spontaneous fission activity could have been due to ^{252}Cf. The number of fissions in the source was frequently measured with polycarbonate films over a period of 3 months after ozonization and gave an average value of 4 ± 0.3 fissions per day over this whole period. Statistical uncertainties made it impossible to determine whether the fission activity was growing or decaying.

After this period a more uniform source was prepared by chemically exchanging the Hg activity onto an evaporated film of PbS on a 240 ± 20 μg cm^{-2} polycarbonate backing. Roughly 50% of the fission activity was transferred onto the PbS film. With this source it was now possible to measure the kinetic energy spectrum of the fission fragments and energy spectra were measured with two silicon surface barrier detectors for both single and coincident summed kinetic energies. The observed spectra are shown in Fig. 1. We also show in Fig. 1 the spectra obtained in the same apparatus from a ^{252}Cf source which was prepared by sublimation of ^{252}Cf onto successive layers of PbS to simulate the HgS–PbS source as closely as possible. Clearly source thickness and non-uniformity could greatly affect the spectral shapes.

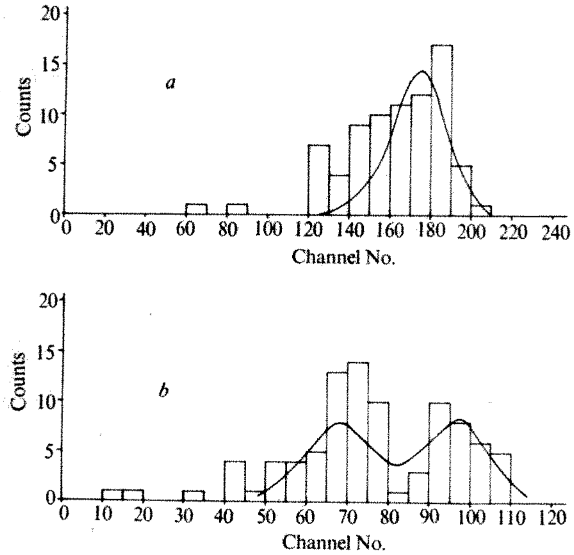

Fig. 1 Energy spectra of fission fragments observed with the mercury source. In *a* the summed kinetic energy spectrum is given, and in *b* the singles spectrum observed with the front detector. The continuous lines show similar measurements with a ^{252}Cf source with much better statistics.

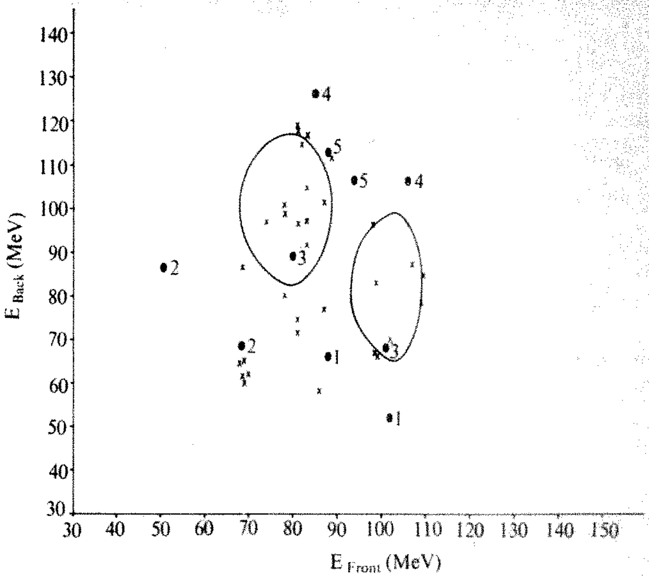

Fig. 2 Correlated energies of fission fragments from the Hg source. The pairs of numbered points show the alternative interpretations when the analysis of the events is ambiguous. The contours enclose the region in which 90% of ^{252}Cf fragments would be found and are asymmetric because of energy loss in the source backing.

Fig. 1*a* shows that the two sum spectra appear to differ in shape particularly in the low energy region and that the Hg sum energy spectrum seems to have a peak at slightly higher energy than that for ^{252}Cf (roughly 194 MeV, as compared with 182 MeV for ^{252}Cf). Because of the difference in spectral shapes, however, the average value of the sum kinetic energy for the Hg source is lower than that of ^{252}Cf. The possibility of non-binary fission cannot be ruled out for superheavy elements, so any conclusions based on the assumption of binary fission must be regarded with caution. In addition, if multiple fission occurs, our two detector system will not in general measure the total energy. With this in mind, it is worthwhile noting that since the total kinetic energies for binary fission are roughly proportional to $Z^2/A^{\frac{1}{3}}$, then fragments from the binary fission of element 112 would be expected to have a total kinetic energy 24% higher than that for ^{252}Cf (or about 225 MeV) whereas those from Hg isotopes would be expected to have a total kinetic energy of about 130 MeV. A statistical χ^2 analysis indicates that the probability that the observed sum spectrum is consistent with that of pure ^{252}Cf is less than 1%. This probability increases to 30% if the point with the largest value of χ^2 (at channels 120–130) is removed from consideration.

The energy spectrum of single fission fragments from the W2 source is shown in Fig. 1*b*. The two peaks in the spectra are in similar positions to those measured for a ^{252}Cf source under the same conditions. The ratio of the heights of the high energy to low energy peaks is $0.7 \pm 0.2 : 1$ for the Hg source compared with a value of 1 : 1 measured for the ^{252}Cf source.

The fission data were printed out sufficiently often that about 50% of the individual singles and coincidence events could be correlated with each other. In these cases, it is possible to determine the energy of the fission fragments striking the back detector by a simple subtraction. The energies of the correlated fragments are plotted in Fig. 2, together with a contour

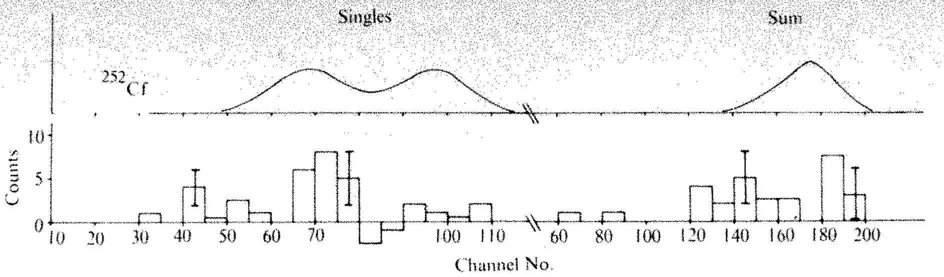

Fig. 3 Fission energy spectra for coincident and singles events after subtraction of a ^{252}Cf kinetic energy spectrum normalized to 70% of the total number of fission counts. Also shown for comparison are spectra obtained with a ^{252}Cf source.

which encloses the region in which 90% of the ^{252}Cf fragments would be found. The relatively large number (30%) of the observed fissions from the Hg W2 source which do not fall within the contours can be regarded as evidence of spontaneously fissioning material other than ^{252}Cf in the Hg W2 source.

Using the same thin mercury source another measurement was made of the ratio of intensity of 6.1 MeV alpha particles to fission fragments. The value obtained was $\alpha/f = 11 \pm 1.5$ to be compared with the known value $\alpha/f = 16$ for ^{252}Cf. If the 6.1 MeV alpha particles are associated entirely with the disintegration of ^{252}Cf this would imply that ~70% of the observed fission activity at that time stemmed from ^{252}Cf.

Using the same W2 mercury source a measurement of the mean number of neutrons emitted per fission ($\bar{\nu}$) was made using the apparatus described by Mather *et al.*[2]. In the present measurements the requirement for a coincidence between the fission fragment and a prompt gamma ray was omitted. The value of $\bar{\nu}$ obtained in this way was 3.7 ± 0.5 which when compared with the known value of $\bar{\nu} = 3.76$ for ^{252}Cf again suggests that a significant fraction of the activity could have been due to this element.

Measurements of the fission energy spectra, the mean number of neutrons per fission and the alpha/fission intensity ratio all suggested that a significant fraction of the observed fission activity from the thin source could have been due to ^{252}Cf. Further chemical separations were therefore carried out on the Hg source from the W2 target to give both mercury and actinide fractions. Measurements of the fission and alpha activity of the resulting actinide source showed that 73 ± 7% of the fission activity observed at the time of the kinetic energy measurements now appeared in the actinide fraction and here the 6.1 MeV alpha to fission ratio was $16 \pm 2 : 1$ indicating that this fission activity was probably due to ^{252}Cf.

With the Hg fraction an attempt was made to exchange the Hg onto a PbS coated film. Approximately 70% of the original Hg tracer and no detectable (< 1%) rare earth tracer were found in this HgS–PbS source. Using a surface barrier detector in the same geometry as for the original source about 3% of the fission activity (1 ± 0.5 per week) was found in the HgS–PbS source. The ratio, α/f, for this source for the few alpha particles observed between 6.05 and 6.15 MeV was found to be $4.7 \pm 4 : 1$. A subsequent 2 week measurement of the fission activity of this source with a polycarbonate film gave no events. The source from the residual solution was too thick to be counted.

From these measurements it appears that approximately 70% of the fission activity now observed from the W2 source is due to ^{252}Cf although the remaining 30% seems unlikely to be due to this element. As early alpha spectra showed smaller amounts of alpha activity having an energy of around 6.1 MeV for comparable rates of fission activity we conclude that after the original separation either the source has been contaminated or the ^{252}Cf has grown in. The frequent changes in source geometry and low counting rate make it difficult to distinguish between these possibilities. It is not possible to explain the changes in alpha to fission ratio as being the result of changes in source thickness as the alpha particles have a range which is larger than that of the fission fragments.

Finally, in Fig. 3 we show the results of the fission energy spectra measurements after subtraction of a ^{252}Cf kinetic energy spectrum normalized to 70% of the total number of fission counts. Within the very large statistical uncertainties of these residual spectra it appears that the total kinetic energy spectrum either shows two peaks (one broad peak centred about 150 MeV and one at about 195 MeV) or one very broad peak (centred at about 170 MeV). The single spectrum shows three regions: two broad regions centred at about 65 and 100 MeV and a sharper and more pronounced peak at 85 MeV.

The Hg W2 source used for the kinetic energy measurements was placed on an Ilford K-1 nuclear emulsion for 13 days before the final chemical separation. Examination of the tracks in this emulsion gave an upper limit of 0.5 non-binary fissions per day (about 30% of the "non-Cf" fissions).

The fact that the measurement of $\bar{\nu}$ for the total Hg source was close to that of ^{252}Cf indicates that the remaining 30% of the fission activity has a neutron multiplicity in the range of 2 to 5. The distribution of multiplicities did not indicate any events of multiplicity 7 or greater and also no large preponderance of events of multiplicity 1.

To summarize, both the alpha to fission ratios and subsequent chemical separations show that at the time of our kinetic energy measurements 70% of the fission activity was due to ^{252}Cf. After subtraction of the ^{252}Cf component the residual fission kinetic energy spectra differ considerably from those of known actinides. An unlikely explanation is that the distribution of kinetic energies could indicate a mixture of spontaneously fissioning species, one in the light Hg-Po-Ra region (but see ref. 3) and one in the heavier No-Lw region. Another possibility is that it could be the spectrum of fragment energies produced in an unusual mode of fission such as predicted by Greiner[4] for superheavy elements. It must be noted that the kinetic energy spectra and the value of neutron multiplicity do not agree with the published predictions for binary fission of superheavy elements; however, neither do the kinetic energy spectra appear to fit those of any known spontaneously fissioning actinide isotope.

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Complete Fusion induced by Krypton Ions: Indications for Synthesis of Superheavy Nuclei

COMPLETE nuclear fusion has been produced by bombarding targets of germanium, cadmium and thorium with 450 MeV Kr^{23+} and 500 MeV Kr^{24+} obtained from the Orsay accelerator ALICE[1]. Recoiling synthesized nuclei were slowed down in helium gas, transferred through a capillary tube and deposited on a steel rod in an evacuated enclosure[2]. An annular silicon semiconductor counter around the capillary tube detected the alpha particles produced by the decaying nuclei. Typical bombardment times were of the order of 10 h with 10^8 Kr ions s^{-1}, and the background was shown to be insignificant by bombarding for 24 h without a target in place. Further tests also showed that secondary neutrons and gamma rays did not induce nuclear reactions in the detector.

The apparatus was tested by carrying out experiments with an argon beam and a dysprosium target[3] that produced the known alpha emitters ^{200}Po and ^{199}Po. Also the reaction $^{84}Kr + ^{74}Ge \rightarrow ^{153}Er + 5n$ was studied and found to give a maximum cross section of 20 mbarn at a bombarding energy of 370 MeV. The total cross section for $^{74}Ge\ (Kr, xn)$ reactions of 32 mbarn was found to be in agreement with theoretical estimates based on the concept of critical angular momentum[4,5]. This shows that the total fusion can be represented by:

$$\sigma_{CF} = \pi\hbar^2 \frac{l_c^2}{2\mu\bar{\varepsilon}}$$

where l_c is the critical value of the angular momentum quantum number, μ is the reduced mass and $\bar{\varepsilon}$ the centre of mass energy. Studies of the reactions $^{116}Cd + ^{84}Kr \rightarrow ^{197}Po + 3n$ at a bombarding energy of 375 MeV and $^{164}Dy + ^{40}Ar \rightarrow ^{200}Po + 4n$ at 190 MeV gave cross sections of 3 mbarn and 25 mbarn, respectively, demonstrating the effect of the enhancement of the fission width because of the larger angular momentum of the krypton projectiles, and the decrease of fission barriers for light polonium isotopes.

After the successful demonstration of the technique and with the confidence placed in the theoretical prediction of the cross sections by the above results we bombarded a thorium target with 450 MeV Kr^{23+} ions for 10 h. No activity was observed—probably because the energy was near the Coulomb barrier—and the experiment was repeated with 500 MeV Kr^{24+} ions on a 1 mg cm^{-2} thorium target. The alpha spectrum obtained at this energy is shown in Fig. 1. Energy calibrations with the thoron deposit (8.78 and 6.05 MeV) and with ^{153}Er (4.67 MeV) and ^{152}Er (4.80 MeV) are shown with larger arrows. Many alpha particles of energy between 7 and 9 MeV have been assigned to light isotopes of polonium, astatine or radon which might have been produced by fission of very heavy nuclei. The absence of ^{212}Po at 8.78 MeV is significant. The peaks at 8.1 MeV, 8.48 MeV might be attri

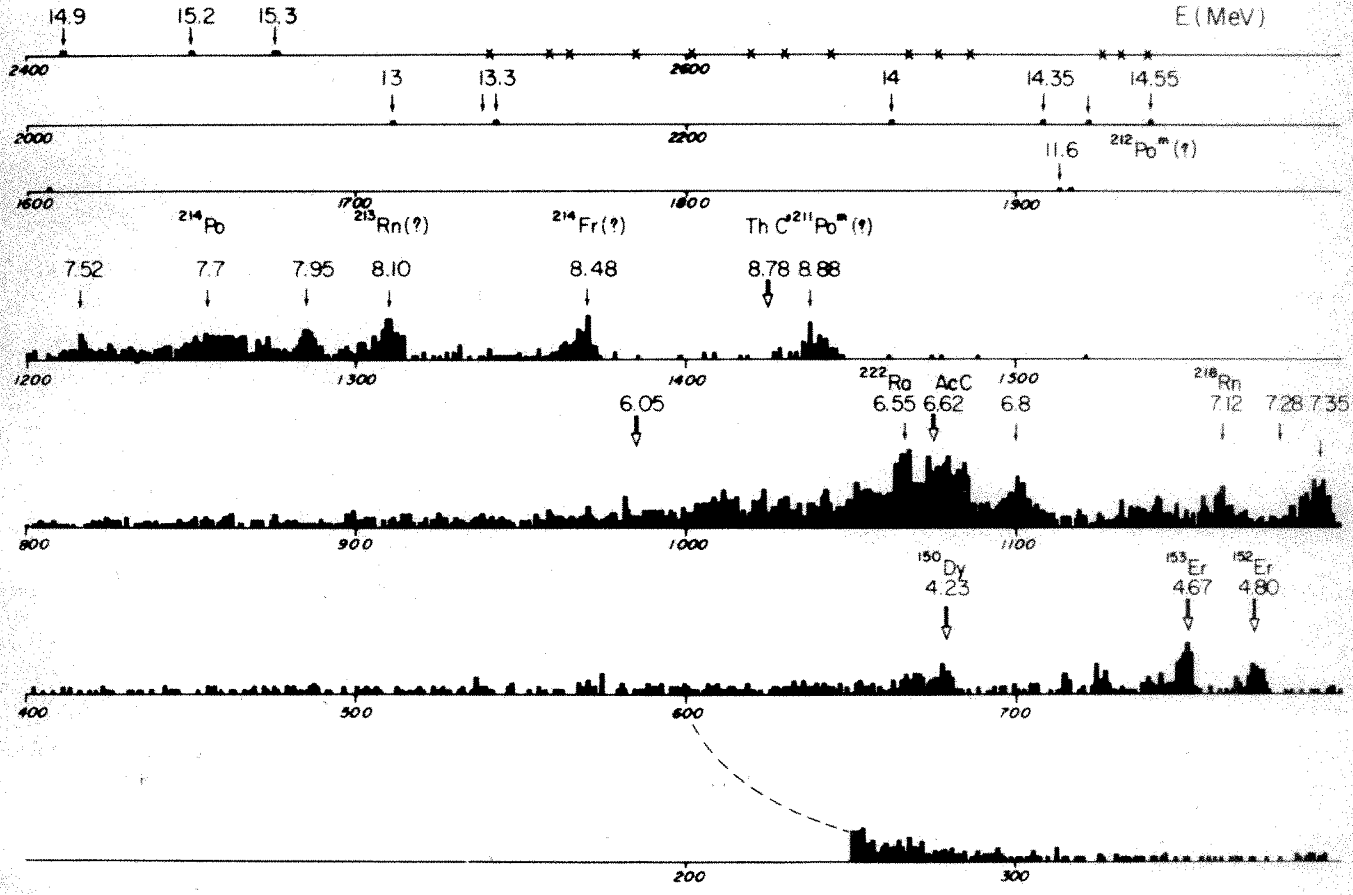

Fig. 1 Pulse height spectrum of particles obtained with a semiconductor annular junction detector. Energy calibration is indicated by large arrows. Crosses represent counts which have been dismissed by the study of the stopping power. (Target ^{232}Th, projectiles Kr^{24+} at 500 MeV.)

buted to isotopes 254 and 256 of element 102. At 8.9 MeV, the alpha rays cannot be attributed to $^{211}\mathrm{Po}^{m}$ since the corresponding 91% branch at 7.28 MeV was not observed. The most significant result is the observation of pulses corresponding to alpha energies higher than 9 MeV, which had not been found at 450 MeV bombardment.

To ensure that the particles responsible for such pulses were indeed alpha particles, a thin aluminium foil was put in front of the detector and the experiment repeated twice for a full bombarding time of 10 h each. By this method several pulses corresponding to energies larger than 16 MeV were dismissed. They were probably the result of coincidences of alpha particles from a nucleus and its daughter when the disintegration half life of the daughter is shorter than the pulse length of 1 μs. The other events have been shown to be due to alpha particles of energies between 13 and 15 MeV. The cross section is of the order of 10 μbarn for the nuclei which emit these particles and their half life lies between 10^{-3} s and 1 min. Because of the conditions under which the alpha particles are produced they might come from superheavy isotopes for which the theory[6] predicts alpha disintegrations of 13 to 14 MeV with half lives of ms. It is not possible to attribute 13 or 14 MeV alpha particles to elements of atomic numbers less than 102 with a half life as long as 1 ms. These results can be taken as an additional indication for the existence of superheavy elements first observed by Marinov *et al.*[7] in a very different experiment.

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Late Precambrian Glaciation: an Anti-Greenhouse Effect?

A GLACIATION in the latest part of Precambrian time[1] is commonly accepted as a major, rapidly waxing and waning event. Most of the northern hemisphere was involved[2].

Before that glaciation major limestone or dolomite bodies are often developed; for example in Finnmark, northern Norway, the original type area for the "Varanger" Glaciation. Here, a Porsanger Dolomite Formation reaches 250 m thick over 60 km outcrop and appears only part of a much larger carbonate body stripped off in the glaciation. Spencer gives full details of similar events in the Scottish Dalradian[3]. These thick carbonate horizons may be linked with sealevel fall; that is, the withdrawal of seawater into ice-caps.

I am now inclined to think that the very thickness of these carbonate bodies[4,5] argues against that idea. And, in my own area, there is preliminary stromatolite evidence taking the age of the lowest part of the Porsanger Formation as far back as 900 m.y.

If the carbonate deposition did not depend on the glaciation, did the glaciation depend on the carbonate deposition? Discussing the development of the atmospheres of Earth, Mars and Venus, Rasool and de Bergh[7] suggest that increase of carbon dioxide in the Earth's atmosphere led to gradual heating.

Rubey estimates that some 6.7×10^{22} g of CO_2 is now locked up in sedimentary rocks. Most of this is presumably Carboniferous, Mesozoic and Tertiary—not late Precambrian. Yet, if there is an important CO_2 threshold effect[7], then perhaps even this less voluminous trapping of the gas in late Precambrian times had serious effects on the temperature, producing a fall of temperature which was a major factor in the onset of the glaciation.

If this glaciation were in some real sense the result of locking up of carbon dioxide, why did this start to happen in the first place? There are three somewhat interdependent alternatives:

(1) Cloud[9] suggests that these were times when an ozone screen first became effective, shielding organisms so that they could colonize open areas. Before, life was restricted in reproduction to sheltered spots, severely limiting photosynthetic activity. A change such as Cloud suggests would produce (*a*) general spread and massive increase, perhaps over 1–200 m.y. of earlier, presumably largely chemautotrophic life (*b*) with increase in population, an enormously enlarged gene pool, with attendant increase in rate of evolution.

Where restricted marine basins developed, there could be great increase in carbonate deposition biologically controlled.

(2) Alternatively, the carbonate bodies developed at this time because this was a phase of extreme peneplanation, such as in much of the Jurassic and Cretaceous. No glaciation followed then.

(3) Valentine and Moores[10] discuss the regulation of sealevel in terms of plate–tectonics. If the rapid plate movements of the past 100 m.y. occurred in Vendian times then the effect on sealevel of those movements may have been very great.

This could be seen as providing the right place for shallow water sediments during the major burst of evolution suggested in (1).

Crowell and Frakes[11], discussing the later Gondwana glaciation, propose that glaciation here was not short-lived but extended through most of Palaeozoic time. Areas were glaciated as they moved across the polar region. According to them, glaciation had more to do with changes in the atmosphere/ocean circulation than anything else. Their proposals cannot be examined here, but it may be that we have accepted a sudden glaciation in late Precambrian times because of its vital role in the stratigraphy of otherwise very confused areas.

The idea of an anti-greenhouse effect should be examined in two ways: (*a*) In the light of local geology—what was the local sedimentary background to the carbonate deposit and the tillites? (*b*) How does it relate to other theories of glaciation, and to the problems of the Proterozoic/Phanerozoic boundary?

The anti-greenhouse effect could be a new argument for rapid onset of the Late Precambrian Vendian glaciation. Crowell and Frakes or, more recently, Crawford and Daily's[12] objections to rapid waxing and waning of the Vendian glaciation seem to be based on comparison with the apparently very different conditions of the Gondwanaland Palaeozoic Glaciation.

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Are the Astrophysical and Statistical Schools of Irreversibility Compatible?

A SERIOUS crisis at the foundations of natural sciences has been generated recently by the astrophysical school of thought[1-4] which maintains that the origin of irreversibility and all time asymmetries observed in nature can be traced back to initial conditions which gave rise to the present expansion of the universe as a whole. The astrophysical school has been considered to be in serious contradiction to the more established statistical school[5] which claims that irreversibility and time asymmetries originate in the nature of macroscopic observations; that is, in the macroscopic instrument which records information and which retains a record of it. I wish to show how both schools of thought are essentially compatible with each other in particular from a cosmological viewpoint of entropy-free thermodynamics[4].

First, I stress, in agreement with Beauregard[6] and Bergmann[7], that the introduction of statistics into the time symmetric laws of (classical or quantal) mechanics does not by itself produce irreversibility. Thus to obtain the statistical time asymmetry one must add a specific postulate of asymmetry, for example, the initial (not final) condition stating that "blind statistical retrodiction is forbidden". Second, I refer to a few broad aspects of the Hogarth–Gold–Narlikar–Gal-Or school of thought[1-4] which explains how the first cosmological asymmetry (Fig. 1) is linked, in a one to one fashion, to all other time asymmetries that are in evidence. In supporting this school of thought Beauregard[8] maintains that if a reflecting box is not expanding, all enclosed quantal systems will keep fluctuating around an equilibrium energy state, exchanging quanta on stationary waves. But if the reflecting box is expanding, all enclosed quantal systems will be decaying and emitting quanta on all sorts of electromagnetic, electronic, neutronic and so on, waves. More specifically Beauregard feels that space expansion goes hand in hand with a general decay of gravitating sub-systems, and general emission of gravitons on the corresponding retarded waves. The last were shown by Narlikar[3] to be generated by the world's expansion (which, in turn, can be traced back to initial conditions imposed on time-symmetrical field equations) out of the time-symmetrical Wheeler–Feynmann theory. As to the microscopic time asymmetry in elementary particles Aharony and Ne'eman[9] have recently demonstrated (for the evolution of the K°–$\bar{K}^\circ$ complex) a one to one relation with the cosmological asymmetry.

According to the statistical school[10], however, any finite region of the universe should have a finite relaxation time and should be in equilibrium—a condition unfulfilled throughout the universe accessible to our observations (note the redshift, Hubble's law, and the irreversible photon expansion into the inter-galactic non-reflecting space). The escape from this contradiction as well as from the Olbers' "paradox" can first be traced to the redshift which operates to diminish the radiation fields. Thus the sky is dark (and thus plays the role of a huge "thermodynamic sink") because in most directions the material on a line of sight is receding. Inside non-expanding galactic bodies, as we know from observations, the transfer

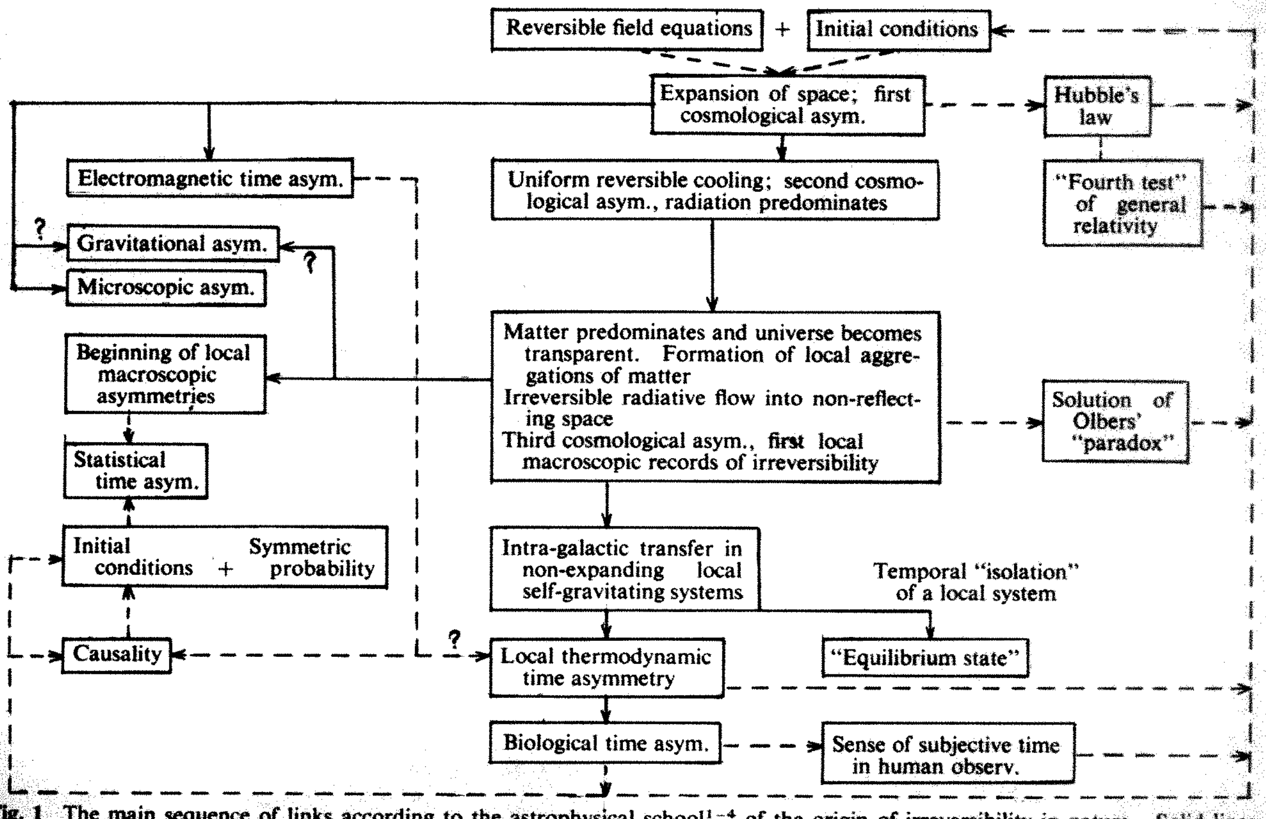
Reversible field equations
+
Initial conditions
Expansion of space; first cosmological asym.
Hubble's law
"Fourth test" of general relativity
Electromagnetic time asym.
Uniform reversible cooling; second cosmological asym., radiation predominates
?
Gravitational asym.
?
Microscopic asym.
Beginning of local macroscopic asymmetries
Matter predominates and universe becomes transparent. Formation of local aggregations of matter
Irreversible radiative flow into non-reflecting space
Third cosmological asym., first local macroscopic records of irreversibility
Solution of Olbers' "paradox"
Statistical time asym.
Initial conditions + Symmetric probability
Intra-galactic transfer in non-expanding local self-gravitating systems
Temporal "isolation" of a local system
Causality
?
Local thermodynamic time asymmetry
"Equilibrium state"
Biological time asym.
Sense of subjective time in human observ.

Fig. 1 The main sequence of links according to the astrophysical school[1-4] of the origin of irreversibility in nature. Solid lines represent expected physical links.

of energy involves a very large number of intermediate stages which include such local processes as conduction, convection, chemical and nuclear reactions. But because the net result is a continuous emission of energy from galactic surfaces any energy released inside them should, eventually, find its way out into the expanding space (which never reaches "equilibrium state"). The time constant for intra-galactic transfer depends therefore on the scale, position and details of the system inside non-expanding galactic aggregations. The time constant of a local system may be estimated in the laboratory by a temporal "isolation" (through imposition of "time-invariant" boundary conditions interacting with external non-equilibrium systems which supply the required energy) during which time asymmetry persists for a while but eventually vanishes. This mechanism explains the occurrence of local "equilibrium states", in an overall non-equilibrium surrounding. It also explains how the first cosmological asymmetry dictates all local processes far away along the world lines.

Yet, very convincingly, the statistical school maintains[5] that irreversibility has its root in the very process of observation or more specifically in the macroscopic instruments which record information. In trying to reconcile the two schools of thought I first raise the question: what might be the earliest possible local macroscopic instrument to record irreversibility in an expanding (or contracting) universe? My lemma is that the origin of irreversibility defined thus can be traced back in time to the period when the first local self-gravitating aggregations of matter had started to form out of an isotropic and uniformly expanding universe. This proposition is based on the assumption that before the formation of local irregularities of matter the universe was uniform with radiation making an overwhelmingly dominant contribution to the pressure (in equilibrium with uniformly scattered nuclei). As the expansion proceeded the uniform temperature fell reversibly (the second cosmological asymmetry). At about 3,000 K electrons were captured by nuclei and remained in bound orbits. At this state they no longer scattered photons and the universe became transparent. Therefore, aside from the problem that we are still far from understanding in detail the formation of self-gravitating aggregations of matter, we arrive at the conclusion that local macroscopic information of irreversibility was not in existence at the earliest period (at least 10^5 years) when there was already at least one clear and dominating cosmological asymmetry. Consequently, to affirm one school and deny the other would result in a contradiction in a non-uniform expanding world; in considering a uniform expanding world, however, the astrophysical school supplies a more universal theory about the original asymmetry of nature and the sequence of relationships which links it to all asymmetries that are now in evidence.

As another example I consider criticism of the astrophysical by the statistical school. This claims that there is no direct evidence for the relevance of cosmological effects on the nature of the viscosity of a gas[11]. Previously[4], I showed how the world's expansion can serve as a point of departure in laying a new basis for the second law of thermodynamics. A new entropy-free thermodynamics was thus constructed in which the second law was derived from the first law. Considering small adiabatically expanding regions with real, viscous media the entropy-free theory reduces to

$$-P_0^c\frac{\mathrm{d}V_0}{\mathrm{d}t}-\frac{1}{\rho}\bar{\bar{\pi}}:\mathrm{grad}\,\bar{v}=\frac{\mathrm{d}U_0}{\mathrm{d}t}=0 \qquad (1)$$

where P_0^c is the proper hydrostatic (or radiation) pressure, V_0 is the specific volume, U_0 the specific internal energy, ρ the total density, $\bar{\bar{\pi}}$ the viscous stress tensor, $\bar{v}$ the centre of mass velocity vector, and t the time. Now for all real gases the adiabatic expansion of space dictates

$$P_0^c\frac{\mathrm{d}V_0}{\mathrm{d}t}>0 \qquad (2)$$

Consequently I obtain

$$\left(-\frac{1}{\rho}\bar{\bar{\pi}}:\mathrm{grad}\,\bar{v}\right)>0 \qquad (3)$$

Assuming Newtonian gases (without specifying the sign of the viscosity) equations (1) to (3) require that

$$\mu=\rho P_0^c\frac{\mathrm{d}V_0}{\mathrm{d}t}(\Phi_v)^{-1}>0 \qquad (4)$$

where Φ_v is the dissipation function which by its mathematical nature is always positive. The world's expansion dictates, therefore, a positive viscosity parameter. Some similar findings can be obtained for non-Newtonian fluids.

In general, the theory I postulated[4] allows one to construct an entirely new and entropy-free thermodynamics in a close analogy to extant, entropy-based, non-equilibrium phenomenological or statistical theories.

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BIOLOGICAL SCIENCES

Reduction of Catechol-O-methyltransferase Activity by Chronic L-Dopa Therapy

THE use of large doses of L-dopa, the immediate precursor of dopamine, in the symptomatic treatment of Parkinsonism has prompted investigation of the effects of this amino-acid on enzymes involved in catecholamine metabolism. It has been found that the activity of enzymes mediating the synthesis of catecholamines, such as tyrosine hydroxylase[1] and aromatic L-amino-acid decarboxylase (personal communication with W. Dairman and S. Udenfriend), diminishes during prolonged L-dopa administration. Conversely, monoamine oxidase, one of the enzymes involved in catecholamine degradation, has been found to increase in the tissues of animals given L-dopa[2] as well as in the serum of patients treated with this drug[3]. We now report a substantial decline in the activity of catechol-O-methyltransferase (COMT), another enzyme important in mediating catecholamine catabolism, in the red blood cells of Parkinsonian patients receiving chronic L-dopa treatment.

Red blood cell COMT activity was assayed[4] on two to ten occasions in seventeen patients. Red blood cell indices, reticulocytes and complete blood counts remained normal in all patients studied. Control subjects (five men and four women with a mean age of 57 yr) had received no drugs for at least 2 weeks before the study. Only one of this group had been exposed to L-dopa, but the drug had been withdrawn 2 months beforehand. Patients in the L-dopa treatment group (three men and five women with a mean age of 58 yr) had received L-dopa for 1–20 months (mean 11.8 months). Two of these individuals were receiving optimal therapeutic doses of L-dopa alone; four were receiving L-dopa in combination with α-methyldopahydrazine (MK 486, Merck Sharp and Dohme), an extracerebral inhibitor of aromatic L-amino-acid decarboxylase, and the remaining two patients had two or more COMT determinations while being treated with L-dopa alone as well as in combination with α-methyldopahydrazine. The dose of L-dopa when given alone ranged from 2.9 to 11.2 g/day (mean 6.0 g/day) and from 0.43 to 4.0 g/day (mean 1.4 g/day) when given with the peripheral decarboxylase inhibitor. Red blood cell COMT activity in control subjects did not differ significantly from levels previously found in normal individuals or in patients with schizophrenia[5]. COMT activity was 40% lower in L-dopa-treated patients (Fig. 1). No difference could be discerned between COMT levels in patients receiving maintenance doses of L-dopa alone or in combination with α-methyldopahydrazine.

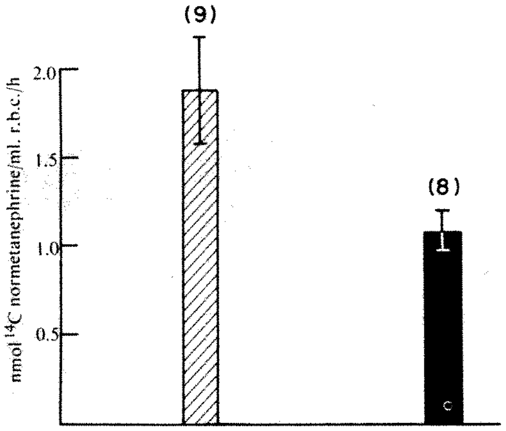

Fig. 1 COMT activity in Parkinsonian patients with L-dopa (black column) and without L-dopa (hatched column) therapy. Values shown are the means (± s.e.m.) of each group. COMT levels were significantly lower in the L-dopa-treated group ($P < 0.05$; Student's *t* test). Blood samples were usually obtained in the early morning. Patient fasted during the preceding 10–12 h. In the treated group, samples were drawn approximately 12 h after the last dose of L-dopa.

The acute effects of L-dopa as well as the effects of duration of therapy were studied in several patients. A single intravenous dose of L-dopa (1 mg/kg) was given to three previously untreated patients. There were no measurable differences in COMT levels before injection or 0.5 and 6 h after injection. Six of the untreated patients (three men and three women) were then given therapeutic doses of L-dopa and studied for 4–16 weeks (Fig. 2). There was a significant reduction in COMT activity by the third week of treatment. By the fifth week, red blood cell COMT levels had decreased to 51% of the level before initiation of L-dopa treatment. In our patients, COMT levels seemed to vary as a function of duration of therapy but were unrelated to total daily dosage. Patients who showed an adequate clinical response to relatively low doses of L-dopa, however, seemed to have a lower COMT activity than those patients requiring relatively large doses.

To assess the specificity of these observations, the effects of L-dopa on the activity of histamine N-methyl transferase and a methanol-forming enzyme were examined. The activities of both of these methyltransferases, assayed according to Axelrod and Cohn[4], were not different from samples from normal volunteers run simultaneously with these patients, or from untreated patients with Parkinsonism.

To investigate the possibility that L-dopa directly influences COMT activity, *in vitro* specimens were pre-incubated for 15 min with 10^{-4} and 10^{-6} M L-dopa. Activity was not significantly altered. Dialysis for 6 h of specimens from L-dopa-treated patients with low COMT activity against 0.005 M phosphate buffer (*p*H 7.5) did not increase COMT activity, excluding the possibility of an easily dialysable inhibitor.

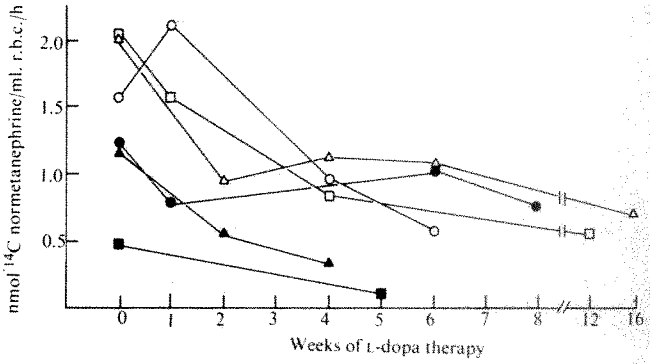

Fig. 2 Reduction in red blood cell COMT activity with L-dopa therapy. Each symbol represents one of the three men and three women studied longitudinally. Age ranged from 52–68 yr (mean = 57). L-Dopa administration was begun at time 0, after initial blood samples were drawn. Patients were studied for up to 16 weeks, during which time COMT activity declined, reaching significance after 2 weeks ($P < 0.05$; Student's *t* test).

Enzyme changes in the anucleate red blood cell may represent a unique situation, not seen in tissues capable of synthesizing new enzyme or substrate. To account for reduced COMT levels in the red blood cell, one must postulate either diminished synthesis by precursors, increased degradation or inhibition of the enzyme. Dialysis experiments have ruled out the presence of a small dissociable inhibitor; the rapidity of decline in COMT activity relative to the normal red blood cell turnover of 120 days argues against diminished enyzme synthesis in red blood cell precursors. The data are most compatible with increased enzyme lability.

Several clinical studies have suggested a tendency for L-dopa dose requirement to decrease over a period of weeks or for the clinical effects of the drug to increase gradually at a fixed dose[6,7]. The finding of reduced red blood cell COMT activity, if representative of the effect of chronic L-dopa treatment on COMT activity in other tissues, may be relevant to this phenomenon.

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Physicochemical Stereospecificity in Taste Perception of α-D-Mannose and β-D-Mannose

THE anomers α- and β-D-mannose differ structurally only in that H and OH at the C_1 atom of the pyranose ring are interchanged. In spite of this apparently minor difference in structure, it has been suggested that the ambiguity of taste perception of D-mannose is due to actual differences in taste between the two anomers of this substance; the evidence presented in support of this view, however, was indirect because insufficient pure β-D-mannose was available for direct taste tests on that anomer[1]. Sufficient pure β-D-mannose was therefore prepared for a direct and statistically reliable comparison. It was found that the subjects reliably reported the α-anomer as sweet and the β-anomer as bitter. As before, the equilibrium mixture was found to be an ambiguous stimulator.

The β-anomer was prepared by dissolving 26 g of α-D-mannose in 15 ml. of water with heating. Glacial acetic acid (15 ml.) was added to the cool syrup and the resulting solution was filtered through finely divided charcoal under reduced pressure. The funnel was rinsed with 10 ml. of glacial acetic acid and the solution was seeded with about 1 mg of β-D-mannose[2]. A little crystal growth was noted after 24 h. Crystallization was allowed to proceed for 6.5 yr with occasional agitation, at which time sufficient (about 2 g) crystalline material was available for analysis and testing. The crystals were removed mechanically from the mother liquid, washed successively with glacial acetic acid and with absolute ethanol, and dried *in vacuo*. Infrared spectra were obtained using the KBr pellet technique. Peaks were found at 1170, 936, 899, 860, 772, 730, 620, and 448 cm^{-1}, corresponding to the characteristic peaks of β-D-mannose[2,3]. For the α-anomer peaks were found at 971, 960, 915, 885, 831, and 812 cm^{-1}, corresponding to the known characteristic peaks of this substance[2,3]. The equilibrium mixture used was that prepared by Steinhardt *et al.*[1], the spectrum of which confirmed that it contained both the α- and β-anomers in the equilibrium ratio.

Subjects for the taste discrimination tests were five males and five females, aged 19–24 yr. Subjects were instructed not to eat, smoke, nor to drink anything but water for 2 h before the taste tests. Each was given six to ten preliminary trials in which taste stimulators of known characteristics were presented for the purpose of subject screening and familiarization with experimental procedures. Dextrose and a dilute quinine solution were used to establish standards for sweet and bitter, respectively, and α-D-mannose containing a trace of β-D-mannose served as an ambiguous stimulus. The criteria for sensitivity and acceptability of the subject were the responses "sweet" to the dextrose and "bitter" to the quinine solution. After acceptable preliminary trials, each subject was given thirteen test trials which included four α-D-mannose samples, four β-D-mannose samples, four equilibrium mixture samples, and one dextrose sample as a control. The samples were arranged in different random orders for each subject and were administered in the solid state to avoid mutarotation. Weights were 14 mg of α-D-mannose, 6 mg of β-D-mannose, 20 mg of the equilibrium mixture, and 20 mg of dextrose. (The amounts of the α- and β-anomers correspond to the ratio in which they occur in the equilibrium mixture.) Tests were conducted using a double blind procedure. On each trial the experimenter placed the test material on the tongue of the subject who was then instructed to manipulate the substance between the tongue and the hard palate. During the test the subjects recorded their taste sensations as a function of time by depressing one of four appropriately labelled buttons on a response indicator and an operations recorder was used to record the responses "no taste," "sweet," "bitter," and "indistinguishable taste". Following each trial, after the "no taste" button had been pressed, the subject rinsed his mouth with water and was given a short rest period before the next trial.

The responses of two subjects were not included in the experimental results: One failed to follow the instructions not to smoke before the test and the other tasted the dextrose control as "bitter".

Table 1 Frequency of Taste Responses to Anomers of D-Mannose and to Dextrose

	Bitter	Sweet	Sweet-bitter	Indistinguishable	Total
β-D-Mannose	30 (93.75%)	0 (0.0%)	2 (6.25%)	0 (0.0%)	32
α-D-Mannose	0 (0.0%)	30 (93.75%)	0 (0.0%)	2 (6.25%)	32
Equilibrium mixture	23 (71.88%)	2 (6.25%)	5 (15.62%)	2 (6.25%)	32
Dextrose	0 (0.0%)	8 (100.0%)	0 (0.0%)	0 (0.0%)	8

Subjects' responses to the substances tested are summarized in Table 1. Each of the responses was coded +1 for sweet, −1 for bitter, and 0 for indistinguishable taste. The mean coded scores for the α- and β-anomers were +0.9375 and −0.9375, respectively. For purposes of statistical analysis it was assumed that the 64 observations made were randomly and independently chosen from 16 normal populations with equal variance. The analysis showed that the specific anomer administered significantly influenced the subjects' reports of their taste sensations ($f=787.5$, d.f. 1/7, $P<0.005$). Thus, subjects very reliably reported a sweet sensation in the presence of α-D-mannose and a bitter sensation in the presence of β-D-mannose.

It seems that the so-called "ambiguity" of taste associated with D-mannose is due solely to the slight difference in the molecular structure between α-D-mannose and β-D-mannose. These results confirm the conjecture that a high degree of physicochemical stereospecificity is exhibited by taste receptors.

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fi⁻ R Factors giving Chloramphenicol Resistance

ALTHOUGH many fi^+ R factors confer resistance to chloramphenicol, fi^- R factors seldom do. Watanabe *et al.*[1] stated in 1964 that all the naturally occurring fi^- R factors which they had studied lacked chloramphenicol resistance. In our laboratory, no fi^- R factor giving chloramphenicol resistance has been observed among several hundred drug-resistant strains of enteric bacteria. In 1968 Watanabe, Furuse and Sakaizumi[2] reported an fi^- R factor (S–a) from *Shigella* which conferred chloramphenicol resistance at about the same level as fi^+ R factors. Aoki, Egusa, Ogata and Watanabe[3] this year described R factors from the fish pathogen *Aeromonas liquefaciens*, which were all fi^- and some of which carried chloramphenicol resistance determinants.

Watanabe[4] found that factor S–a exhibited no superinfection immunity with any of several fi^+ or fi^- R factors.

We wish to report that S–a and two of Watanabe's R factors from *A. liquefaciens* carrying chloramphenicol resistance (our designations RA3 and RA4) constitute in *Escherichia coli* K12 a new compatibility group which we propose to call W (for Watanabe).

Factor S–a confers resistance to streptomycin (S), chloramphenicol (C), kanamycin (K) and sulphonamides (Su). Both RA3 and RA4 confer resistance to S, C and Su.

Evidence for the new compatibility group is presented in Tables 1 and 2. The W factors are not excluded by and can coexist stably with an F-like R factor, R136, an I-like R factor, R64 (ref. 5), the P-type factor, RP4 (ref. 6), N-type R factors, N3 and R46 (ref. 7) and two R factors from *A. liquefaciens*, RA1 and RA2, not at present assignable to any compatibility group. Transfer of a W factor was not inhibited by the presence of another W factor in the recipient, but, in every colony tested, led to the dislodgment of the resident factor. Thus surface exclusion, seen with other groups of plasmids, was apparently absent but even temporary coexistence was not demonstrated.

The two C-sensitive derivatives of J53(S–a) (Table 2) retained all other resistances (S, K and Su). One such J53 (S–aC^s) segregant was used as recipient in matings recorded in Table 1. All three factors of the W group lose resistance to chloramphenicol at a high rate. Thus, although all members of this group so far identified confer chloramphenicol resistance, the discovery of W factors without this marker may be predicted.

Since these R factors seem to constitute a group distinct from other R factors so far tested their resistance genes may perhaps have a different evolutionary origin. To test this we are trying to show whether they determine a chloramphenicol inactivating enzyme similar to that of fi^+ factors[8,9]. The kanamycin resistance of S–a is unusual. All other R factors examined in our laboratory, which determine kanamycin resistance, confer a high level (> 500 μg/ml.) of resistance to kanamycin and also neomycin and paramomycin resistance, but not gentamicin resistance[10]. Such a pattern results from inactivation by phosphorylation[11,12]. S–a gives low-level resistance to kanamycin (J53R⁻ is inhibited by 1 μg/ml., J53(S–a) by 20 μg/ml.), low level resistance to gentamicin (J53R⁻ is inhibited by 1 μg/ml., J53(S–a) by 5 μg/ml.) and none detectable to neomycin or paramomycin, a pattern which may result from inactivation by acetylation[8,12,13]. It may be that this pattern of aminoglycoside resistance is unique to the W class.

Table 1 Transfer Frequency

Donor *	Recipient *	Compatibility of R factor in recipient	Transferred resistance (chloramphenicol)	Selection for Transferred resistance (chloramphenicol) and resident resistance (tetracycline † or kanamycin)
J62(S–a)	J53		10^{-3}	—
J62(S–a)	J53(RA1)	A?	4×10^{-4}	3×10^{-5}
J62(S–a)	J53(RA2)	A?	8×10^{-4}	4×10^{-5}
J62(S–a)	J53(R64)	I	10^{-3}	10^{-4}
J62(S–a)	J53(R46)	N	4×10^{-4}	5×10^{-5}
J62(S–a)	J53(N3)	N	10^{-4}	10^{-5}
J62(S–a)	J53(RP4)	P	5×10^{-4}	5×10^{-5}
J62(RA3)	J53		2×10^{-3}	—
J62(RA3)	J53(RA1)	A?	9×10^{-4}	8×10^{-4}
J62(RA3)	J53(RA2)	A?	2×10^{-3}	4×10^{-4}
J62(RA3)	J53(R64)	I	2×10^{-3}	5×10^{-4}
J62(RA3)	J53(R46)	N	2×10^{-3}	10^{-4}
J62(RA3)	J53(N3)	N	8×10^{-4}	10^{-4}
J62(RA3)	J53(RP4)	P	2×10^{-3}	3×10^{-3}
J62(RA3)	J53(S–a)	W	2×10^{-3}‡	0
J62(RA3)	J53(R136)	F	10^{-3}	2×10^{-4}
J62(RA4)	J53		10^{-3}	—
J62(RA4)	J53(RA1)	A?	2.5×10^{-3}	10^{-3}
J62(RA4)	J53(RA2)	A?	2×10^{-3}	9×10^{-4}
J62(RA4)	J53(R64)	I	4×10^{-3}	7×10^{-4}
J62(RA4)	J53(R46)	N	2×10^{-3}	2×10^{-4}
J62(RA4)	J53(R15)	N	10^{-3}	—
J62(RA4)	(RP4)	P	4×10^{-3}	2×10^{-3}
J62(RA4)	(S–aC^s)	W	2×10^{-3}+	0
J62(RA4)	(R136)	F	5×10^{-3}	5×10^{-4}

* J62 and J53 are nutritionally distinguishable strains of *Escherichia coli* K12 F⁻.

† Counts on tetracycline-containing plates are generally lower than on plates without tetracycline, even when all bacteria in the inoculum carry genes for tetracycline resistance.

‡ 50 recipient colonies tested. In all, the transferred R factor was present, the previously resident one was lost.

Table 2 Stability of R Factors Singly and in Pairs

Strain	Resistance markers	Compatibility group	No. of colonies tested Total	T^s	C^s
J53(S–a)	SCKSu	W	211	—	2
J53(RA3)	SCSu	W	181	—	1
J53(RA4)	SCSu	W	62	—	0
J53(R64)	ST	I	40	0	—
J53(N3)	STSu	N	152	0	—
J53(R46)	ASTSu	N	40	0	—
J53(RP4)	ATK	P	40	0	—
J53(S–a)(R64)		W+I	137	0	0
J53(Sa)(R46)		W+N	298	0	1
J53(S–a)(RP4)		W+P	849	0	1
J53(S–a)(RA1)		W+ ?	612	0	4
J53(RA3)(R64)		W+I	84	0	0
J53(RA3)(N3)		W+N	76	0	1
J53(RA3)(R46)		W+N	20	0	0
J53(RA3)(RP4)		W+P	20	0	0
J53(RA3)(RA1)		W+ ?	23	0	0
J53(RA3)(S–a) *		W+W	0	—	—
J53(RA4)(R64)		W+I	116	0	0
J53(RA4)N3)		W+N	20	0	0
J53(RA4)(R46)		W+N	37	0	0
J53(RA4)(RP4)		W+P	148	0	1
J53(RA4)(RA1)		W+ ?	16	0	0
J53(RA4)(S–a) *		W+W	0	—	—

* No clones available to test (see Table 1).

Kanamycin used was 'Kantrex', kanamycin sulphate, from Bristol Laboratories Ltd. Gentamicin was 'Genticin', gentamicin sulphate from British Schering Ltd.

Note added in proof. Not all fi^- R factors determining chloramphenicol resistance belong to group W. R57b (Witchitz, J. L., and Chabbert, Y. A., *J. Antibiot.*, **24**, 137–139; 1971) and R387 (unpublished observation) are fi^-, give chloramphenicol resistance and are compatible with S–a.

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Compatibility Groups among *fi*$^-$ R Factors

TRANSMISSIBLE R factors in bacteria are divisible into two main classes, *fi*$^+$ (fertility inhibition$^+$) and *fi*$^-$, according to their effect on F mediated conjugation[1]. *fi*$^+$ R factors determine F-like pili[2]. Some *fi*$^-$ R factors determine pili similar to those specified by col I (I-type pili)[3] which can be recognized as receptors for I-specific phages like If1 (ref. 4). Although heterogeneity among *fi*$^-$ R factors has already been indicated[5–8], it is sometimes assumed that all *fi*$^-$ R factors have I pili[9,10].

Among 26 *fi*$^-$ R factors examined by Lawn *et al.*[2], twenty determined the production of I-type pili. Strains of *Escherichia coli* K12 carrying the other six R factors (of which one example was R46) permitted no increase of I-specific phage If1 and so by this criterion give no evidence of having I-type pili. We find that the classical *fi*$^-$ factors, N3 and R15 (ref. 1), also fail to allow multiplication of I-specific phage. Other examples of *fi*$^-$ R factors which do not allow multiplication of I-specific phage in *E. coli* K12 are RP4, derived from a strain of *Pseudomonas aeruginosa*[11], and S–a[12,13].

One of the ways in which plasmids are classified is by superinfection immunity: bacteria carrying one plasmid hinder the entry of others of the same group (surface exclusion) and also two plasmids of the same group will not coexist stably in the same host (incompatibility)[14].

By these criteria, most *fi*$^+$ R factors constitute one class of plasmid. These also characteristically produce pili similar to those of the sex factor F. By the same criteria the *fi*$^-$ plasmids are heterogeneous. Those which determine I pili constitute one superinfection immunity class. N3, R15 and R46 belong to another which we propose to call N. RP4 represents a third[11] and S–a a fourth[13].

Table 1 Frequency of Transfer

Donors	Resistance markers	Recipients	Compatibility group of resident R factor	
J62(R144–3)	K	J53		2.7
		J53(R64)	I	0 ($< 10^{-7}$)
		J53(R46)	N	4.6
		J53(N3)	N	1.1
J62(R64)	ST	J53		1.8×10^{-3}
		J53(R44)	I	0 ($< 10^{-7}$)
		J53(R46)	N	1.5×10^{-3}
		J53(RP4)	P	1.8×10^{-3}
J62(RP4)	ATK	J53		3.3×10^{-3}
		J53(R144)	I	1.4×10^{-2}
		J53(R64)	I	3.0×10^{-3}
		J53(R46)	N	1.4×10^{-3}
		J53(N3)	N	2.4×10^{-3}
J62(N3)	STSu	J53		2.2×10^{-3}
		J53(R144)	I	3.0×10^{-3}
		J53(R46)	N	7.2×10^{-5}
		J53(RP4)	P	3.8×10^{-3}
J62(R46)	ATSu *	J53		2.1×10^{-3}
		J53(R44)	I	3.3×10^{-3}
		J53(N3)	N	2.2×10^{-5}
		J53(RP4)	P	2.0×10^{-3}

The frequency of transfer is expressed as the number of R+ recipients after 1 h at 37° C/No. of R+ donors.

A, Ampicillin; S, streptomycin; T, tetracycline; K, kanamycin; Su, sulphonamide.

* R46 carries resistance to ASTSu but in these experiments a spontaneous, non-reverting segregant, giving no resistance to streptomycin, was used.

The evidence for their division into classes is shown in the tables. Table 1 shows the frequency of transfer of R factors of groups I (R144–3 and R64), N (N3 and R46) and P (RP4) to recipients with or without resident R factors. Selection was made with antibiotic to which the donor, not recipient, was resistant. Where colonies developed, they were subcultured, and tested for the continued presence of all markers of both factors. After growth in drug-free broth, the stability of markers of each R factor was examined by replica plating or, sometimes, by streaking out individual colonies (Table 2). Watanabe demonstrated surface exclusion in matings between strains carrying R15 and N3, but did not test for their stable coexistence. Since N3 determines resistance to streptomycin, tetracycline and sulphonamides, while R15 determines streptomycin and sulphonamide resistance, one cannot directly demonstrate the existence of R15 in the presence of N3. We transferred N3 to K12(R15), selecting for tetracycline resistance; we used the recombinant strains as donors in matings with recipients, selecting for streptomycin resistance, and screened the recombinants for tetracycline resistance. From two of the donor strains, all recombinants tested were tetracycline resistant, while from the third, most (fifty-seven out of sixty-three) were tetracycline-sensitive. This suggests that the two factors do not coexist stably.

Table 2 Stability of R Factors Singly and in Pairs

Strain	Resistance markers	Total replicated	No. of colonies No growth on plates containing A	S	T	K	Su
J53(R144)	K	50	—	—	—	0	—
J53(R64)	ST	1,000	—	0	—	—	—
J53(RP4)	ATK	217	—	—	0	0	—
J53(R46)	ATSu	132	1	—	1	—	1
J53(N3)	STSu	817	—	0	2	—	0
J53(R144)(R64)		0					
J53(R64)(RP4)		1,298	—	0	—	0	—
J53(R144)(R46)		226	7	—	7	2	7
J53(R144)(N3)		2,267	—	2	—	0	—
J53(RP4)(R46)		281	—	—	—	0	0
J53(RP4)(N3)		102	1	0	1	1	0*
J53(R46)(N3)		144	93	50	—	—	—

Abbreviations are as in Table 1.

* One strain had lost RP4 and T^R from N3.

The tables show that exclusion of one I-like factor by another is complete, whereas with the N group of plasmids, frequency of transfer to a host already carrying a related plasmid is reduced about 100-fold or less[1]. Coexistence, however, does not last through many generations, and the plasmid which is most frequently retained is that whose resistance marker has been selected in the cross. Growth in drug-free medium leads to symmetrical loss, about half the clones retaining each one.

Guerry and Falkow (personal communication), in studying R factor homology by DNA hybridization, found that N3 shows no measurable homology with the I group factors R64, R144 or col I nor with any *fi*$^+$ plasmid. Khatoon and Iyer[8] have isolated a new sex factor specific phage, whose indicator strain carries a naturally occurring, derepressed R factor RM98. Strains carrying R46 or N3 propagate this phage but strains with F or I pili so far tested do not (Iyer, personal communication), so it seems likely that the N group of plasmids determine specific pili (or other surface structure) different from F or I pili.

Some confusion has arisen because those *fi*$^-$ R factors most studied in Japan[1] belonged to the N group, and those studied most extensively in England[2] were I-like plasmids.

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Quantitative Method for assessing One Symptom of the Withdrawal Syndrome in Mice after Chronic Morphine Administration

FEW quantitative methods exist for assessing the effects of withdrawing morphine from addicted laboratory animals. The aim of the experiments described here was to assess whether a method which depends on the number of characteristic vertical jumps made by mice after morphine withdrawal[1] could be used as a measure of the withdrawal syndrome. This simple method has now been found to give reasonably repeatable and consistent results.

If nalorphine, a narcotic antagonist, is injected into mice which have been chronically injected with morphine, it precipitates a withdrawal syndrome which includes hypermotility, tremors, diarrhoea, micturition and piloerection[2]. The "intensity" of the syndrome was rated by Huidobro and Maggiolo on a five-point scale, but each point on their scale comprised a number of different symptoms which varied in frequency and intensity in different mice[3]. Recently Way and his colleagues reported a simple quantal method; they determined the proportion of mice which leapt off a raised platform during 15 min after the injection of the antagonist naloxone[4]. With our method, which was developed independently, a measure of frequency, instead of an all-or-none measure, can be obtained from each mouse, and an 8 min observation period has been found adequate for most purposes.

More than 300 female mice of a T.O. strain (18–22 g) were used; injections were subcutaneous and doses are expressed in mg/100 g body weight throughout.

In the first experiment morphine sulphate was injected once daily at 1000 h; 1 mg was given on the first day, and this was increased by 1 mg daily. After 4 days of injections the mice were divided into three groups. Group 1 received 4 mg/day for the rest of the experiment. In group 2 the dose continued to be increased by 1 mg/day and in group 3 it was increased by 4 mg/day (Fig. 1*a*). To precipitate a withdrawal syndrome, nalorphine (1 mg) was injected into eight mice from each group 5 h after the daily morphine administration. The mice were then placed singly in enclosed rectangular ($12 \times 8 \times 15$ cm) 'Perspex' containers. The number of jumps made by each mouse was counted in an 8 min period which began 3 min after the nalorphine injection. A "jump" was defined as any response by a mouse in which all four feet were off the ground at the same time. Vigorous vertical jumping usually began about 3 min after the injection of the antagonist. Mice were only used once and the results are shown in Fig. 1*b*.

There were marked differences between the mean scores of the three groups, though there were also considerable individual differences within each group. In group 1 the number of jumps remained at the low level reached after the fourth injection. The distribution of scores was, however, markedly skewed because some mice did not jump at all. Non-parametric statistical tests were therefore used throughout[5]. Group 2 jumped significantly more often (Mann-Whitney U-test: $P < 0.01$) than group 1 after both 8 and 10 days. The results from groups 2 and 3 show that by day 8 a greater number of jumps occurred ($P < 0.001$) in group 3, whose dose was increased more rapidly, than in group 2. It seems that where the dose is increased by an equal amount daily the intensity of the precipitated jumping is proportional to the amount of morphine injected.

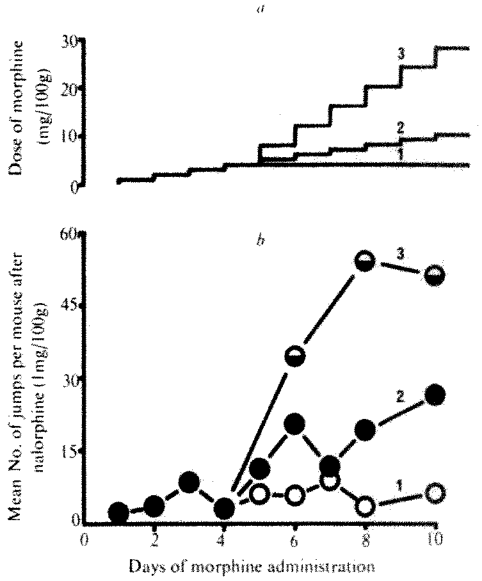

Fig. 1 The intensity of the withdrawal syndrome in mice given one daily injection of morphine. *a*, The ordinate shows the dose of morphine given at each injection (mg/100 g). All mice received morphine on a regime increasing by 1 mg/100 g (from 1 mg/100 g) for the first 4 days. Then group 1 continued to receive 4 mg/100 g at each injection; group 2 had the dose increased by 1 mg/100 g/day; group 3 increased by 4 mg/100 g/day. *b*, The effect of these different dose regimes on the average number of jumps over 8 min in groups of eight mice. Jumping was precipitated by 1 mg/100 g of nalorphine. Group 1 (○) remained at a low level of jumps. Group 2 (●), with a small dose increment, jumped more than group 1 but less than group 3 (◒), the latter having a higher dose increment.

In other experiments morphine was injected three times daily (0900 h, 1300 h and 1700 h). Group 1 received 5 mg at each injection. Group 2 was given doses of 5, 5 and 7.5 mg of morphine in the first three injections and each of these was then increased by 2.5 mg/day. The higher dose at the third daily injection was to minimize any overnight withdrawal effects. Control animals received saline three times daily. Jumps were then counted after an injection of nalorphine, as before.

Fig. 2 shows that initially there was a rise in the number of jumps produced in both groups 1 and 2. Significant differences ($P < 0.05$) were obtained between control and morphine-treated mice from the second day of the experiment onwards. After 4 days (twelve injections) group 1, which was receiving a constant dose of morphine, made fewer jumps while group 2, which was on an increasing dose schedule, continued to show an increase in jumps. It was therefore not possible to obtain a consistent quantitative relationship between the number of jumps and the total dose when a constant amount of morphine was injected.

These results suggest that to obtain an increase in the severity of the withdrawal syndrome, as reflected in the number of jumps, morphine must be injected on an increasing dose schedule.

To confirm that the jumping which occurred in the precipitated abstinence syndrome was due to drug withdrawal, another group of mice which had received morphine three times daily for 4 days merely had their injections stopped but no antagonist was given. Jumping again occurred with a maximum between 14 and 24 h after the last morphine injection. Greater variability was seen during the abstinence syndrome compared with the antagonist precipitated withdrawal syndrome.

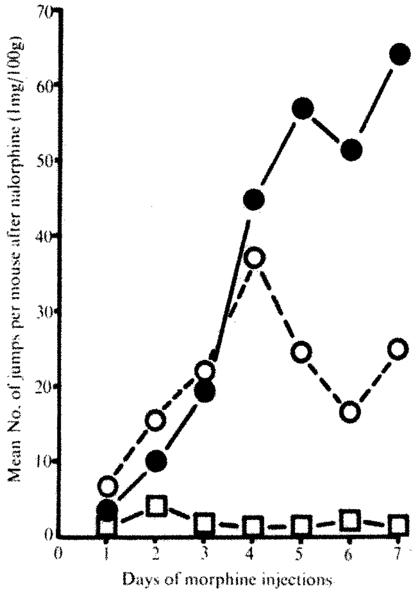

Fig. 2 The effect of a constant or increasing dose regime and the intensity of the withdrawal syndrome in mice given morphine three times daily. The ordinate shows the mean number of jumps, following an injection of nalorphine (1 mg/100 g) in groups of eight mice over 8 min. Group 1 (○) received 5 mg/100 g morphine at each injection and at first the number of jumps increased but later fell. Group 2 (●) was injected with morphine on an increasing dose schedule (see text) and the average number of jumps continued to increase throughout the experiment. Little jumping was seen in control mice given saline three times daily (□).

Jumping has also been correlated with other forms of behaviour following the withdrawal of morphine from mice. For example, the number of jumps seems to be positively correlated with faecal output in the nalorphine-induced abstinence syndrome. This result is in agreement with work using morphine-addicted rats[6]. A decrease in body weight is one sign of morphine withdrawal in rats[7-9], but has not been observed in mice[10]. In mice injected as our group 2, however, a body weight loss does occur on discontinuation of morphine treatment. This is positively correlated with the time course of jumping during the abstinence syndrome.

This method of looking at the number of jumps made by each mouse following the precipitation of a withdrawal syndrome by a narcotic antagonist enables differences between regimes of morphine administration to be detected using small groups of animals. If groups of mice are given the same morphine treatment but, for example, different pretreatments, the effects of the latter on the number of jumps can also be investigated. Thus the method can be used to study quantitative aspects of the development of physical dependence on morphine[11]. Second, the number of jumps might be used as an index of the addiction liability of a new drug. It could also be used to determine whether a drug can prevent an abstinence syndrome in morphine treated mice.

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Verbal Communication with L-Dopa Treatment

DURING the past 2 years we have studied the action of L-dopa in drug-induced Parkinsonism[1], true Parkinsonism[2] and psychosis[3]. In all investigations we found numerous behavioural aberrations. Here, however, we discuss the beneficial effect of L-dopa on verbal communication.

Placebo was given for 1 week and then replaced by oral L-dopa for 2 weeks, in a dose of 1 g in the first week and 2 g in the second week. All patients remained on their previous neuroleptic medication throughout the study to yield a reliable and steady behavioural base line. Ten of the original fourteen patients were given the Kent-Rosanoff word association test. (The four patients excluded were deficient in the English language.) Response time and the responded word were recorded immediately after the stimulus word was presented. If the patient's response was in the top 75% of the frequency

Table 1 Verbal Communication as Total Percentage

Patient	Neuroleptic medication	1 g of L-dopa	2 g of L-dopa
A.B.	88.8	92.5†	92.5†
R.D.	22.2	25.9†	25.9†
C.E.	77.7	81.4	88.8†
M.G.	37.0	44.4†	40.7
R.H.	66.6	81.4†	74.0
N.L.	77.7†	74.0*	77.7†
W.M.	70.3	81.4	88.8†
T.O.	62.9	81.4†	81.4†
J.P.	70.3	88.8†	81.4
R.W.	44.4	59.0	70.3†

$P=0.011$. * Hallucinated when tested. †Highest score patient obtained through study.

Table 2 Communication Response Time in Seconds

Patient	Neuroleptic medication	1 g of L-dopa	2 g of L-dopa
A.B.	1.5	1.3	1.2*
R.D.	4.6	2.0	1.9*
C.E.	2.4	2.0	1.4*
M.G.	4.7*	5.1	5.9
R.H.	4.1	1.9	1.5*
N.L.	2.8	2.1	1.9*
W.M.	3.0	2.8	2.2*
T.O.	2.9	2.3	1.8*
J.P.	2.1	1.7	1.6*
R.W.	1.2*	1.2*	2.0

$P=0.055$. * Fastest response time for patient through study.

table for the presented stimulus word, it was considered communicable. Finally, all responses were added to yield a total of communicable and noncommunicable responses and their percentages were calculated.

Nine patients significantly improved verbal communication with L-dopa treatment (binomial test, $P=0.011$); there was an optimal dose for some. No significant difference was obtained for the 1 and 2 g doses when individually compared for improvement and only three patients communicated best for both doses. The patient whose communication did not improve with L-dopa treatment was observed to hallucinate while receiving L-dopa. Verbosity in all patients improved to the extent that some spontaneously reported their hallucinations.

Eight patients responded to stimulus words faster when L-dopa was administered, and two responded slower (binomial test, $P=0.055$), and when the 1 g and 2 g doses are compared the fastest and slowest scores all occur with 2 g (binomial test, $P=0.001$). The two patients who responded more slowly with L-dopa treatment, however, improved their verbal communication.

It is known that dopamine and noradrenaline, for which dopa is the precursor, resemble stimulant drugs in their action. These catecholamines are located in the brain stem at the sites of action of the stimulant drugs, such as amphetamine. L-Dopa may thus stimulate the lethargic, withdrawn patient. Improved verbalization may be helpful in the psychotherapy of noncommunicative patients: we have therefore initiated a preliminary trial of L-dopa in autistic patients.

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Drug Use and Grades in College

ONE of the most compelling arguments against illegal drug use, especially by the young, is that it instills in the user an "amotivational syndrome" of apathy, lethargy and loss of motivation in the conventional sense[1]. The argument assumes that drug use tends to become routine and that the drugs specifically prohibited by law are associated with reduced achievement-oriented behaviour. Given the fact that drug use is currently at an all-time high among the young—and possibly more so among society's talented young than in any other group—these issues deserve empirical exploration. The latest Gallup poll, conducted in December 1970, indicated that in a roughly random sample of American college students, 42% had tried marijuana at least once. Moreover, this was an increase of almost 1% per month from previous surveys.

During January and February 1970, I distributed a brief questionnaire to about 560 students attending my deviance and delinquency classes at the State University of New York at Stony Brook. Since these classes are not representative of the student composition of the university of which they are a part, I regard these data as exploratory rather than definitive. About seven students in ten had smoked marijuana at least once in the preceding 6 months. Roughly three in ten had used an amphetamine in the preceding 6 months to become "high"; this was the second most popular drug taken. Heroin was one of the least often tried or used drugs in the survey, with only 4% of the students taking it at least once in the preceding 6 months. But these figures exaggerate the importance of all drugs apart from marijuana because they were chiefly used on a very episodic and experimental basis. Roughly 85–90% of all recorded episodes of drug use reported by the sample involved marijuana alone and only slightly more than one instance in ten of illegal drug use involved the combined use of any and all drugs apart from marijuana. It is therefore misleading to discuss the drugs used on the college campus as if they were used with equal frequency. The phenomenon is chiefly one of marijuana use.

The median level of marijuana use was 1.0 times per week. Since the average length of a marijuana "high", or intoxication, is about 3 h, the typical user is under the influence of this drug for roughly 4 h per week, that is, 3–4% of his waking hours. It is therefore difficult to imagine how marijuana could generate a significant loss in motivation, given its relatively small space in the typical user's temporal life, unless the recent studies, which indicate that drugs containing THC may have long term effects, are taken into account[2].

After making the crude distinction between the total abstainer and the student who had used marijuana once or more, I found that their grades were almost identical: 32% of the marijuana experimenters and 33% of the total abstainers had a "B" grade point average or better. This is obviously well within the range of random fluctuation, but a more detailed analysis of users yields an interesting relationship obscured by the gross dichotomization between the user and the non-user. There seems to be a curvilinear relationship between marijuana use in the preceding 6 months and grades earned. The highest grades were earned by the casual and infrequent marijuana smoker, and the lowest by the heaviest user; the abstainer earned only slightly higher grades than the heavy user. Only 29% of the daily marijuana users had achieved a B average or better, and 31% of the abstainers did as well. But 45% of those smoking three or four times a month and 47% of those smoking once or twice a month had the same average (Table 1).

If the number of drugs the student experiments with at least once in his lifetime is used as another indicator of drug involvement, there seems to be no difference between the grades of the abstainer and those of the student who has tried, at least once, between one and three drugs. But grades decreased significantly when I examined the student who had tried four or more different kinds of drug. There were 10% fewer students with a B average or better in this group (Table 2).

The same result is obtained when specific drugs are used as a measure of drug involvement. Only 12% of the heroin experimenters (those students who have tried heroin once or more in their lives, a category which includes addicts), the lowest percentage of any group, had a B average or better, while 32% of the total sample, 32% of the abstainers and 32% of mari-

Table 1 Average Grades by Frequency of Smoking Marijuana in Preceding 6 Months

	Straight B or higher	C+ to lower than B	Lower than C+	Total %	N
Every day	29	35	35	99	31
3–6 times/week	24	40	36	100	58
1–2 times/week	23	43	34	100	88
3–4 times/month	45	27	27	99	51
1–2 times/month	47	32	21	100	57
Less than once per month	31	50	19	100	48
Never	31	43	25	99	157

Table 2 Average Grades by Total Number of Different Drugs Ever Tried (or "Experimented With") in One's Lifetime

	Straight B or higher	C+ to lower than B	Lower than C+	Total %	N
None	32	44	24	100	140
One	36	39	26	101	160
Two or three	35	42	24	101	110
Four or more	24	37	39	100	103

juana smokers obtained a B average. Of those who had taken cocaine or methedrine, only 17% obtained a B average or better. Thus it seems that the harder drugs are associated with low grades but that marijuana has no impact at all on grades. Nearly all heroin, cocaine and methedrine experimenters had tried a wide range of other types of drug, but marijuana users varied in their involvement with other drugs—from using none to using nearly all available drugs—and so they represent the broad spectrum as regards grades as well. Marijuana users as a whole have average grades (Table 3).

Table 3 Average Grades by Ever Tried Various Drugs at Least Once in One's Lifetime

	Straight B or higher	C+ to lower than B	Lower than C+	Total %	N
Total sample	32	41	27	100	561
Total abstainer	32	44	24	100	140
Marijuana	32	40	28	100	360
Opium	31	47	22	100	36
Mescaline	29	38	33	100	115
Amphetamines	28	39	34	101	116
LSD	22	40	39	101	96
Barbiturates	22	41	36	99	58
Cocaine	17	62	21	100	29
Methedrine	17	53	31	101	36
Heroin	12	65	24	101	17

The original curvilinear relationship between marijuana use and grades seems applicable to various groups and social categories. It holds for men and women considered separately, for upper-classmen, freshmen and sophomores, and for students from all social classes. The break in grades came at the point at which marijuana was used weekly or more. Of those smoking marijuana less than once a week there was a higher percentage with a B average or better compared with the abstainers, the difference being just over 7%. The abstainer was more likely than the student smoking once a week or more to have a B average, the difference here being less than 7% (Tables 4–6).

Table 4 Average Grades by Marijuana Use in Preceding 6 Months, holding Sex Constant

	Straight B or higher	C+ to lower than B	Lower than C+	Total %	N
	Men				
Never	21	42	37	100	62
Less than weekly	31	40	29	100	80
Weekly or more	15	44	41	100	111
	Women				
Never	39	43	18	100	95
Less than weekly	47	37	15	99	99
Weekly or more	41	37	22	100	63

Table 5 Average Grades by Marijuana Use in Preceding 6 Months, holding Class in College Constant

	Straight B or higher	C+ to lower than B	Lower than C+	Total %	N
	Juniors and seniors				
Never	35	45	21	101	78
Less than weekly	39	40	21	100	98
Weekly or more	22	47	31	100	68
	Freshmen and sophomores				
Never	30	44	26	100	73
Less than weekly	42	37	22	101	79
Weekly or more	26	36	37	99	107

Table 6 Average Grades by Marijuana Use in Preceding 6 Months, holding Father's Occupation Constant

	Straight B or higher	C+ to lower than B	Lower than C+	Total %	N
	Professional and executive				
Never	39	39	22	100	54
Less than weekly	53	35	12	100	66
Weekly or more	31	36	34	101	59
	Sales and clerical				
Never	31	40	29	100	52
Less than weekly	38	40	22	100	63
Weekly or more	23	42	35	100	77
	Manual labour				
Never	26	48	26	100	46
Less than weekly	28	35	38	101	40
Weekly or more	17	44	39	100	36

These data suggest that the amotivational syndrome is far from inevitable—or even typical—in illegal college drug use and that it may be associated only with heavy drug use. But the data do not show whether the relationship between grades (as a measure of achievement) and drug use is a biochemical, a psychological or a sociocultural phenomenon, or whether drug users in college are a preselected group as regards academic potential; some minimal degree of drug use could conceivably lower their grades to the level of their less talented abstaining peers. Moreover, the data do not show whether the relationships described and analysed here have any relevance for very different populations such as the very young, or residents of slum areas.

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Morphological and Cytochemical Effects of Marijuana Cigarette Smoke on Epithelioid Cells of Lung Explants from Mice

THERE have been many experimental studies on the chemical constituents responsible for the hallucinogenic effects of marijuana[1,2], but we know of no reports on the biological effects of marijuana cigarette smoke on the respiratory tract. We have been interested for some years in the biological effects of fresh cigarette smoke, particularly its role in malignant transformation in the respiratory tract of intact animals[3] and in cultured lungs[4]. We have now compared the effects of smoke from cigarettes with and without marijuana.

We used the model system developed for exposing lung explants to puffs of fresh cigarette smoke in standardized conditions[5,6]. Lung explants from Snell's and C57BL mice were prepared on coverslips and exposed in a Filtrona CSM12 smoking machine to puffs of fresh cigarette smoke. Cigarettes were prepared with tobacco alone and with the same tobacco mixed with marijuana (0.5–1 g) in a powder form. We used two types of marijuana, one containing 0.4% tetrahydrocannabinol (THC) and one containing 4% THC. Altogether experiments were carried out on more than 400 lung explant cultures. For each experiment a minimum of eight sets consisting of twenty-four coverslips with matched lung explants was used. Each set comprised a control culture not exposed to cigarette smoke, a culture exposed for 5 consecutive days to two puffs (8 ml. at intervals of 58 s) of cigarette smoke without marijuana, and a culture exposed in the same manner to two puffs of fresh cigarette smoke with marijuana. Media were changed immediately after each exposure with the exception that, after the fifth exposure, media were changed only after 1 h. Cytological characters and chromosomal behaviour during mitosis were studied in live cultures under phase contrast, and in the original unsquashed stained cultures 6–240 h after exposure. The mitotic index expressed as a percentage was obtained by counting all mitotic figures and relating them to the total number of cells of each monolayer grown on the coverslip. DNA metabolism was examined by autoradiography and Feulgen microspectrography[5–7]. All results were reproducible, and were the same for lung cultures from Snell's and C57BL mice.

There were differences between control cultures and those exposed to cigarette smoke with and without marijuana (Table 1). Cigarette smoke alone was cytotoxic[4] after four puffs, while cigarette smoke with marijuana had little cytotoxicity (Table 1) perhaps because after the addition of marijuana, which is a sticky resin, the cigarette smoke had a larger side-stream, so that less smoke *per se* reached the culture. After 24–48 h of exposure to ten puffs of marijuana cigarette smoke, the shape of epithelioid cells and nuclei was affected. After exposure to cigarette smoke alone, these characters were rarely different from those of controls (Fig. 1*a* and *b*), but after exposure to marijuana cigarette smoke, a considerable number of nuclei were unusually large with large nucleoli, which were often in close proximity to each other (Fig. 1*c*), and had a tendency to fuse. Furthermore, although in control cultures and cultures exposed to cigarette smoke alone, the outgrowing epithelioid cells formed a monolayer showing respectively more or less contact inhibition (Fig. 1*a* and *b*), there was a marked tendency to criss-cross formation and piling up of cells after exposure to marijuana cigarette smoke. This indication of abnormal proliferation was accompanied by an increase of mitotic index and by stimulation of DNA synthesis. Although the increase in mitotic index after exposure to cigarette smoke alone was not statistically significant compared with that of the controls, that after exposure to marijuana cigarette smoke was, compared with both controls ($P = 0.0005$) and cultures exposed to cigarette smoke alone ($P = 0.025$). Lagging of chromosomes in metaphase and anaphase was relatively frequent after exposure to marijuana cigarette smoke (Fig. 1*d*). A further detailed chromosomal analysis is planned to see whether marijuana cigarette smoke evokes chromosomal abnormalities in the epithelioid cells of the lung explant. The increase of nuclear sizes after marijuana cigarette smoke was accompanied by a marked increase in DNA content of the epithelioid cells. While in control cultures even the largest nuclei (which, because of their scarcity, had to be sought) contained only rarely 4 DNA $\left(\text{ratio } \frac{2\,\text{DNA}}{4\,\text{DNA}} \text{ of } \frac{10}{1}\right)$, cultures exposed to cigarette smoke without and with marijuana had a higher frequency of nuclei with 4 DNA. Although the

Table 1 Comparison of Effects of Fresh Smoke from Cigarettes without and with Marijuana (0.4% Tetrahydrocannabinol) on Morphology, Mitotic Index and DNA Synthesis in Epithelioid Cells of Lung Explants from Snell's and C57BL Mice

Type of experiment	Cytotoxic effects	Abnormalities in size and shape of cells	Mitotic index ($n_1 = 54$)	DNA content (Feulgen microspectrography) ($n_2 = 450$) Mean ratio of frequency of nuclei $\frac{2\,\text{DNA}}{4\,\text{DNA}}$	DNA synthesis (^{3}H-TdR) ($n_1 = 15$) Frequency of labelled cells
Control	0	0	0.28 ± 0.07	$\frac{10}{1}$	10.9 ± 2.1
Cigarette smoke without marijuana	+ +	(+) − +	0.39 ± 0.002	$\frac{8}{1}$	13.6 ± 2.6
Cigarette smoke with marijuana	(+)	+ +	0.6 ± 0.11 $p\text{Co} = 0.0005$ $p\text{Ci} = 0.025$	$\frac{2}{1}$ $p = 0.0005$	19.2 ± 1.9 $p\text{Co} = 0.01$ $p\text{Ci} = 0.05$

(+), Doubtful; (+) − +, slight effect; + +, pronounced effect.
n_1, Number of cultures examined; n_2, number of cells measured.

ratio $\frac{2\text{ DNA}}{4\text{ DNA}}$ of $\frac{8}{1}$ found after exposure to cigarette smoke alone was not statistically significant compared with that of the controls, there was a striking increase in nuclei with 4 DNA after exposure to marijuana cigarette smoke, resulting in a ratio $\frac{2\text{ DNA}}{4\text{ DNA}}$ of $\frac{2}{1}$, which was highly statistically significant.

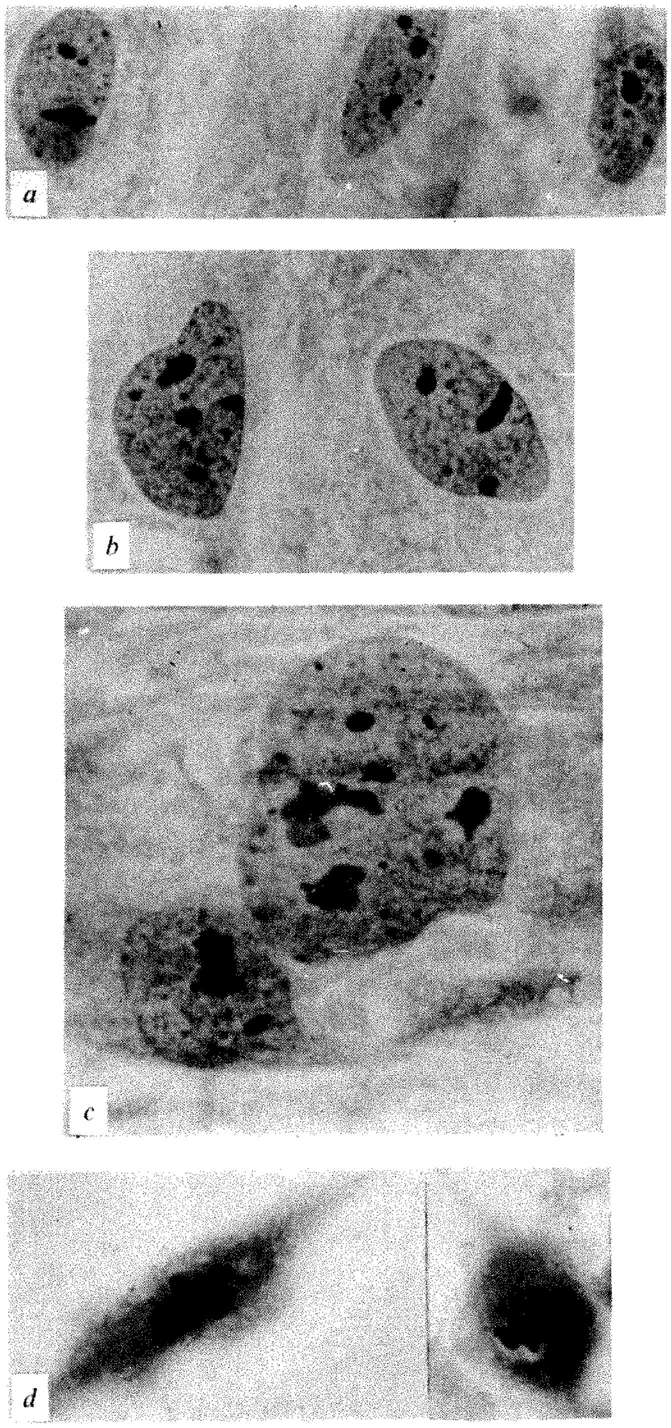

Fig. 1 *a*, Epithelioid cells in monolayer of 15 day old Snell's mouse lung explant, stained with haemotoxylin and eosin. Note well separated uniform nuclei (× 1,000). *b*, The same culture as in *a*, but 72 h after five exposures to two puffs of cigarette smoke without marijuana. Note larger and more irregular nuclei than in *a*. *c*, The same culture as in *b*, but 72 h after five exposures to two puffs of cigarette smoke with marijuana (0.4% THC). Note larger and more irregular nuclei than in *b*. Note also close proximity of nuclei, suggesting fusion. *d*, Metaphases of epithelioid cells in 14 day old C57BL mouse lung explant, 72 h after five exposures to two puffs of cigarette smoke with marijuana. Note lagging of chromosomes.

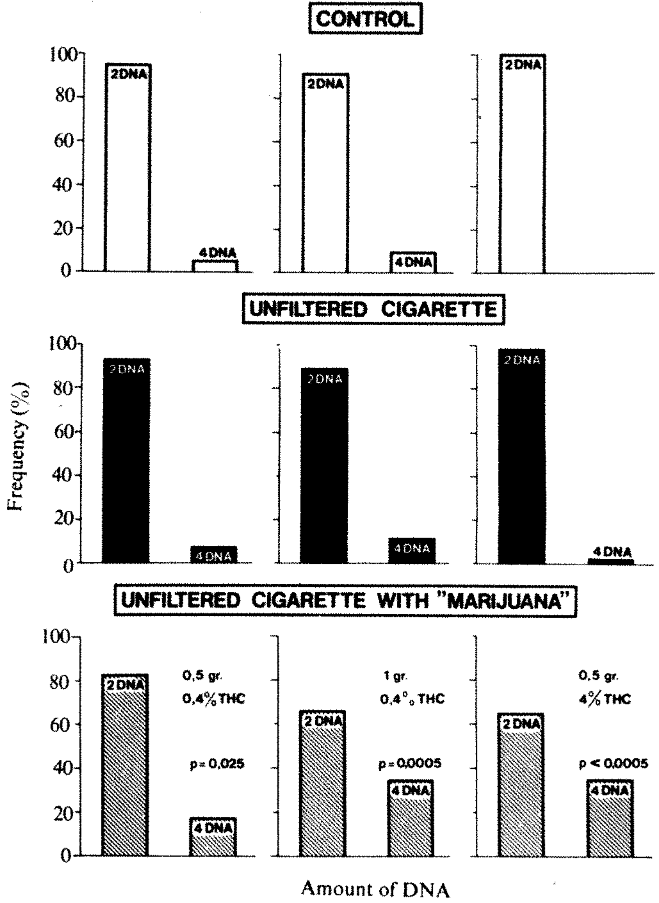

Fig. 2 Comparison between effects of fresh smoke (two puffs daily for 5 days) from one unfiltered cigarette, with and without different doses of marijuana and THC, on the DNA content of epithelioid cells ($N_1 = 1{,}200$) from lung explants of Snell's mice ($n_2 = 3$). n_1 = number of cells measured; n_2 = number of experiments. DNA content was determined by Feulgen microscopy.

A greater effect of cigarette smoke with marijuana than that of cigarette smoke without marijuana was also noted when DNA synthesis was studied by incorporation of tritiated thymidine (^{3}H-TdR). Although after cigarette smoke without marijuana the increase in frequency of labelled epithelioid cells was not statistically significant compared with that of controls, the augmentation in frequency of labelled cells after cigarette smoke with marijuana was statistically significant.

It thus seems that the addition of marijuana to cigarettes produces a smoke which evokes morphological and cytochemical alterations in epithelioid cells of lung explants, such as atypism, mitosis and DNA synthesis, to a significantly higher degree than does smoke from cigarettes without marijuana. Whether the effect of marijuana is due to THC, which is responsible for the hallucinogenic effect, cannot be decided at present. This needs further study on lung cultures with THC itself. Nevertheless our observation, that increasing concentrations of THC in marijuana cigarette smoke evoked earlier and more marked alterations, including higher DNA content, suggests that THC is at least partly responsible for the alterations. When lung explants were exposed to smoke from cigarettes with 4% THC marijuana, the number of epithelioid cells with 4 DNA was seventeen times greater than after exposure to cigarette smoke without marijuana (Fig. 2). On the other hand, when lung explants were exposed to smoke from cigarettes with 0.4% THC marijuana only, the number of 4 DNA cells was only two to three times greater than after exposure to cigarette smoke alone. Regardless of whether THC or other cannabinols are directly involved, the finding that cytological and cytochemical alterations evoked by cigarette smoke were intensified when marijuana was added is noteworthy. These data are of special interest in the light of reports that users of marijuana in Western countries, such as the United States, prefer smoking marijuana cigarettes to eating marijuana itself[1,2].

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Biological Level of Organization of the Chesowanja Robust Australopithecine

A PARTIAL cranium of an australopithecine has been described by Carney, Hill, Miller, and Walker[1] from Chesowanja in Kenya, a new Pleistocene locality which has been dated between 1.1 and 1.2 million years. The explicit statement, both written and in the reconstructions in this report, that the Chesowanja cranium is a large brained robust australopithecine—an evolutionary novelty as far as the robust lineage is concerned—is of considerable importance. I interpret the evidence differently.

My discussion here of the skull is within the descriptive framework provided by Carney *et al.* As these authors correctly recognized, the Chesowanja cranium (KNM-CH-1) shows unmistakable signs, both in its facial construction and in its dental morphology, that it is closely related to the robust australopithecines of Swartkrans, Kromdrai, Olduvai, and other African localities. Before discussing the morphology and the inferred functional interpretation of the cranium, I would like to list briefly the preserved parts of KNM-CH-1. Although it is not mentioned in Carney *et al.*'s report, in addition to the small frontal fragment, the partial cranium was found in two large pieces several feet apart. These two parts are the top of the right face which includes the crushed orbit and the maxillary part of the face which includes the right dentition without the incisors. The specimens were fitted and glued together, and the missing parts were replaced with a white filler. Carney *et al.* state that on the specimen: "Distortion is slight and consists chiefly of folding of the right orbital plate by lateral pressure, and slight flexion of the hypophyseal fossa that is probably associated with this deformation. . . . The base of the cranium, especially in the midline, has been cracked and crushed, and it is the least well preserved part".

I take a slightly different view concerning the mode of preservation of this specimen. After examining it I concluded that it was subjected to, and altered by, great pressures after burial and before exposure. This major deformation of the skull, overlooked by Carney *et al.*, fundamentally affects the interpretation of the cranium. The maxillary part of the skull, although it is undoubtedly correctly fitted to the facial part of the fossil as far as the preserved specimen is concerned, has an altered relationship to the superior part of the face, compared with the presumed condition before burial. The present (post-burial) conformation of the partial cranium seems to be the result of not only lateral pressure, in addition to fairly extensive crushing, shown by the mosaic nature of the bone, but the palate was also pushed inferiorly and slightly anteriorly. This resulted in the alteration of the occlusal surface of the specimen compared with the preserved parts.

Carney *et al.* note (page 514) that the zygomatic process arises from a very anterior and a very inferior position from the maxilla, and they state that this "would have the effect of aligning the anterior attachment of the superficial fibres of m. massseter as tangential to the curve of Spee as possible". The zygoma of SK 13/14 also has its "roots" very low on the maxilla, approximately to the same degree as in KNM-CH-1, distinctly lower than the origins of the zygoma on SK 48.

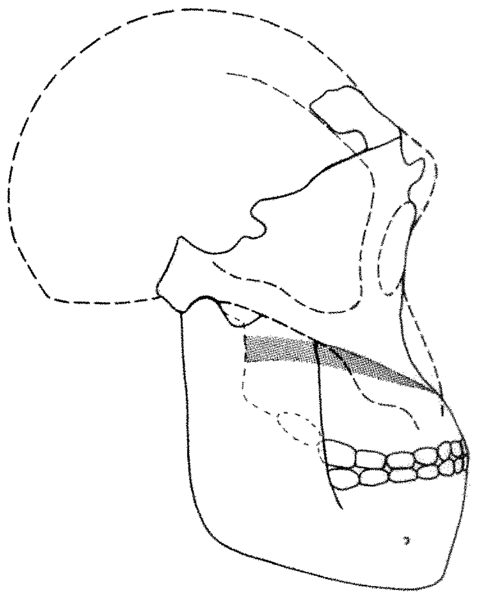

Fig. 1 Reconstruction of the Chesowanja robust australopithecine KNM-CH-1, as presented by Carney *et al.*[1], fitted with the corpus of the Peninj mandible from Lake Natron. The ramus was drawn after the teeth of the Peninj mandible were matched in size with those of the Chesowanja specimen. The stippled area on the cranium represents a segment of the fossil interpreted to be the result of deformation.

Carney *et al.* also state that the "postorbital constriction in KNM-CH-1 is not nearly as great as seen in the other robust australopithecine specimens". They do not mention that the veracity of this statement is dependent on, first, the lateral positioning of the frontal fragment as shown by these authors, and, second, on the assumption that all known robust australopithecines, regardless of sex, share the extensive postorbital constriction displayed by OH 5 and the various pertinent Swartkrans specimens. Before drafting their article, Carney *et al.* had the opportunity to examine the robust female cranium collected by R. E. F. Leakey[2].

Carney *et al.* imply a substantial brain increase for the Chesowanja robust australopithecine cranium. The frontal view in their Fig. 3 shows a reconstructed calotte which not only rises high above the brow ridges (following the line of the fitted frontal fragment), but is also laterally expanded, well beyond the proportions of any robust or gracile australopithecine. This figure can be compared with the stage represented by the Choukoutien loc. 1 hominids (Weidenrech's reconstructions, in the American Museum of Natural History) approximately 400,000 years ago. In addition to the reconstruction, Carney *et al.* comment that "KNM-CH-1 has clearly much bigger anterior and middle cranial fossae than in Olduvai Hominid 5 or as seen in SK 1585 natural endocast". I have also made the comparisons but I could not arrive at an objective judgment because of the badly folded and crushed condition of the cranial fossae of KNM-CH-1.

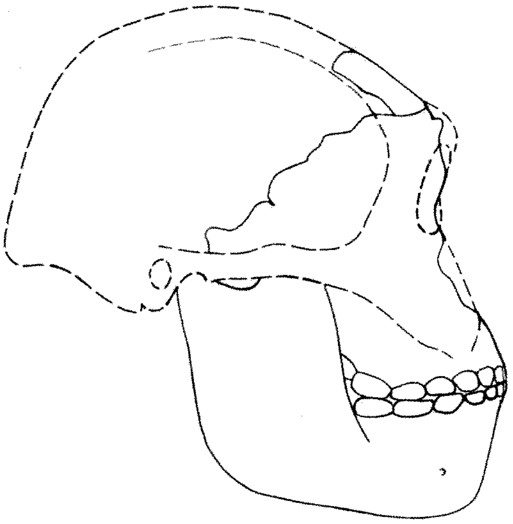

Fig. 2 New reconstruction of the partial Chesowanja cranium. The stippled area of Fig. 1 is excised and the frontal fragment is refitted. Matching the teeth of the Peninj mandible to those of the skull resulted in a perfect fit of the ramus into the space allotted by the reconstruction. This reconstruction of KNM-CH-1 closely resembles the female robust australopithecine KNM-ER-732 collected by R. E. F. Leakey[2].

To test my observations I fitted the reconstruction of Carney *et al.* with the horizontal ramus and dentition of the Peninj mandible. I then proceeded to add the ascending ramus according to the space allotted by the original reconstruction of the skull (Fig. 1). The resulting mandible has a substantially higher ascending ramus than either the Peninj or the SK 23 mandibles. I then prepared a reconstruction based on my interpretation of KNM-CH-1. This differed from Carney *et al.*'s reconstruction in having a slightly different orientation of the hemi-skull, the placement of the frontal fragment in a more medial position and the excision of a segment from the lateral profile shown by stippling in Fig. 1. This part of the skull, as noted earlier, represents what I believe was a part deformed by the movement of the lower face inferiorly and slightly anteriorly. I placed the frontal fragment above the brow ridges more medially than shown by Carney *et al.* in view of the presence of the median supraorbital depression. To this lateral cranial outline I then fitted the Peninj mandible and, in contrast to Fig. 1, the height of the ascending ramus then corresponded to the new facial height of KNM-CH-1. I fitted the mandible after the stippled segment of Fig. 1 was taken out of the lateral outline; the fitting was thus independent of the assessment of the degree and mode of deformation.

If correct, Carney *et al.*'s reconstruction of KNM-CH-1 suggests that besides an apparent great increase in the size of the brain, there was an increase in the distance between the plane of the tooth row and the plane of the temporomandibular joint. The Chesowanja australopithecine would thus be better equipped for herbivorous grinding than any known hominid. The relatively very small canines may be regarded as signs of extreme graminivorous adaptations, but they may also be indicative of the sex of the specimen. I prefer the view that the Chesowanja cranium is a female robust australopithecine, and that it does not show convincing evidence that it represents a large brained evolutionary lineage.

I thank R. E. F. Leakey, L. S. B. Leakey and Margaret Leakey at the Kenya National Museum, P. V. Tobias at the Witwatersrand University and C. K. Brain and Elizabeth Voight at the Transvaal Museum for their hospitality, and A. Hill and A. Walker for discussions. The figures were prepared by Anita J. Cleary. This work was supported by the Wenner-Gren Foundation for Anthropological Research.

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Sampling Variation of Reported Results

BAKAN[1] suggests there is a relationship between birth order and lefthandness. Specifically, the high risk births (defined there to be the first born and the fourth or later birth) are more prone to be lefthanded.

A survey of 321 university students, made as a statistical exercise in the conducting of a sample survey, rather than for medical implications, is shown in Table 1. (The χ^2 values are calculated using Yate's continuity correction.)

Table 1 Handedness and Birth Order

	All		Male		Female	
Birth order	R	L	R	L	R	L
1, 4+ (high risk)	168	21	97	10	71	11
2, 3 (low risk)	115	17	69	7	46	10
	$\chi^2=0.09$		$\chi^2=0.05$		$\chi^2=0.22$	

The results are clearly not significant and do not support the hypothesized relationship between birth order and handedness.

This result is, in itself, unremarkable and the problem is whether it can or should be considered by itself. Surveys of this nature on this fairly simple idea or on closely related ideas may well have been carried out before, possibly frequently. Before discarding these results it is worth asking how many other sets of results have been similarly discarded, either because the research worker thought he was pursuing "an unprofitable line of research" or because an editor thought the results "uninteresting". If selection of results to be published operates, as to some extent it must, then reported results and particularly probabilistic statements referring to significance levels must be interpreted accordingly. If, for example, fifteen experiments are performed to detect a relationship which is not present, the probability that one or more experiments will give a result significant at the 0.05 level is 0.54.

How then shall the scientific world be kept informed of the weight of negative evidence? Some information is clearly necessary so that an estimate can be made of the bias in published significance levels. It is obviously impractical for journals to publish results of all experiments, whether positive or negative. A possible solution to the problem could be that where a journal publishes some results, short notes are encouraged about similar experiments, whether or not these have yielded positive results.

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Unusual Tonoplast in Conifer Leaves

I HAVE found a type of tonoplast in conifer leaves that has not been reported before. Its characteristics suggest that this plasma membrane may be involved in stress resistance in plant cells.

Leaves and bark cortex of various woody species were cut by hand with a razor blade into sections about 1 mm square and 100 µm thick, prefixed in buffered (*p*H 7) 6% glutaraldehyde for 24 h, and then stained with either 5% $KMnO_4$ (*p*H 7) for 7 min at 20° C or 2% OsO_4 (*p*H 6.8) for 3 min at 7° C. Sections were passed through graded ethanol–water solutions to 100% dehydrated ethanol[1], then to propylene oxide, two changes of 15 min each, to propylene oxide–epon (1 : 1), and to epon (D.E.R. 332 and 732) as outlined by the manufacturer (Polysciences, Rydal, Pennsylvania). Thin sections were cut with an MT2 Sorvall ultramicrotome, mounted on uncoated copper grids, and observed with an RCA EMU-4A electron microscope using a 50 µm objective aperture at 50 kV.

A layer, 0.4–1.0 µm thick, between the main vacuole and the cytoplasm was observed in leaf chlorenchyma cells of *Picea pungens* Engelm. and *Juniperus virginiana* L. (Fig. 1). This layer is unusual because the tonoplast in higher plant cells, including those of woody plants, is generally recognized to consist of a single membrane (for example, ref. 2). Since the layer stains with OsO_4 as well as with $KMnO_4$, lipid seems to be present[3]. No such layer was found in the living cells of the leaf stele. There was no apparent seasonal variation in the occurrence or thickness of the layer, which might be expected if it were related to seasonal changes in cold resistance. Heat treatment (57° C for 30 s in summer) disrupted the layer into irregular globules distributed along the outer edge of the main vacuole, again suggesting a lipid nature. The layer does not seem to be an amorphous mass or of artefactual origin, for it sometimes was bounded by a membrane on the vacuole (inner) side (Fig. 1, upper right). Another embedding procedure, using 'Vestopal'[1], also revealed the layer in spruce leaves.

A limited survey of other conifers, including *Pinus strobus* L., *Tsuga canadensis* (L.) Carr., *Taxus baccata* L., and *Thuja occidentalis* L. revealed the presence of a similar but thinner layer. In *Thuja* leaves, it was often lacking, and it was not present at all in leaves or bark of broadleaved trees such as *Fraxinus americana* L., *Ulmus americana* L., and *Acer saccharum* Marsh.

Somewhat similar tonoplasts, or layers adhering to the tonoplasts, have been observed in lower plants[4], but not in higher (tracheophytous) plants, as far as I know. The fact that the layer is thickest in the two most drought-resistant species (*J. virginiana* and *P. pungens*) suggests that it may have some advantage for the leaf in water retention. When leaves of these two species were slowly dried to 35% of the original fresh weight in 3 days, chloroplast lamellae and mitochondrial cristae often disintegrated or lysed while tonoplasts (including the thick layer reported here) usually remained intact. This supports the electron microscope findings in *Drosophyllum*[5] and *Zea mays*[6], which indicate the great sensitivity of cytoplasmic organelles to dehydration. All of this supports the old observation[7] that the tonoplast can remain intact after injury to the cytoplasm.

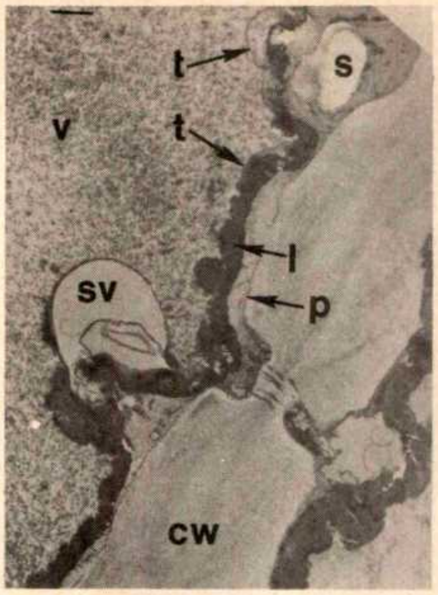

Fig. 1 Part of a chlorenchyma cell of *Picea pungens* together with part of an adjacent cell. l, Layer of lipid-like material; t, inner membrane (perhaps tonoplast) bounding lipid-like material; v, central vacuole; sv, small vacuole (an apparently similar one occurs below the pit, lower right); cw, cell wall (of two adjoining cells); p, plasmalemma; s, starch. A pit with plasmodesmata appears in the cell wall. $KMnO_4$ stain. Bar at upper left represents 1 µm.

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Localization of Nitrogen Fixation in *Anabaena*

THE function of heterocysts in blue-green algae has been controversial for some time; there are indications that these enlarged cells are the site of nitrogen fixation[1,2]. But non-heterocystous blue-green algae may fix nitrogen if grown under low oxygen tension[3], so that heterocysts are not essential for nitrogen fixation in these algae. According to a current hypothesis[4], in aerobic conditions nitrogen fixation is confined to heterocysts, while in anaerobic or semi-anaerobic conditions the vegetative cells fix nitrogen as well. We have evidence to support this view.

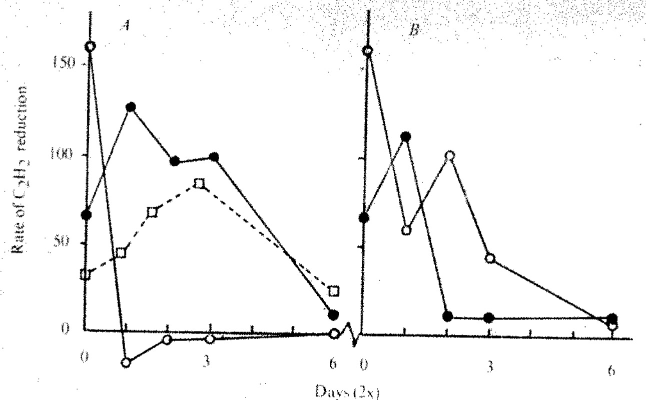

Fig. 1 Oxygen sensitivity of acetylene reduction after readmission of N_2 to an N-starved culture of *Anabaena*. A nitrogen-starved culture (grown under $H_2+5\%$ CO_2 for 5 days) was incubated at t=0 under air+5% CO_2 (*A*) and $N_2+5\%$ CO_2 (*B*). Ethylene production was measured gas chromatographically after 30 min incubation of samples under air+10% C_2H_2 (●), and under He+10% C_2H_2 (total). O_2 sensitive C_2H_2 reduction (○) is plotted as total minus O_2 resistant rate. Aerobic C_2H_2 reduction during the normal growth cycle of an aerobic culture (□) is also shown in *A*. Rate of C_2H_2 reduction was normalized on a chlorophyll basis

$$\left(\frac{\text{nmol } C_2H_2/\text{ml.}/30 \text{ min}}{A(680 \text{ nm}-740 \text{ nm})/\text{cm}}\right)$$

and plotted against time after readmission of nitrogen.

One of the first obvious effects of nitrogen starvation in blue-green algae is the disappearance of phycobilin pigments, which normally constitute about 15% of the dry weight. The continuation of some growth and chlorophyll synthesis during starvation suggests[5] that phycobilins serve as a reserve source of nitrogen. We have studied the pattern of synthesis of one phycobilin, phycocyanin, after readmission of nitrogen to cultures starved of the element.

Cultures of *Anabaena cylindrica* (Cambridge Culture Collection No. 1403/2a) were grown in the medium of Allen and Arnon[6], and gassed with 5% carbon dioxide in air. Phycocyanin was observed by its autofluorescence and absorption under the microscope. Fluorescence was excited with a high pressure mercury arc from which the 546 nm line was isolated by a filter combination consisting of Balzers Calflex C and Corning CS 4-96 (2) and CS 3-368. Phycocyanin fluorescence was isolated with a Balzers B-40 632 nm and a Schott AL 638 interference filter, transmitting a band of 7 nm halfwidth at 632 nm. In cells of *Chlorella* no fluorescence could be seen in these conditions, so chlorophyll fluorescence is negligible at this wavelength. The absorption image was studied with the filter combination used for isolating the fluorescence. A phycobilin-free culture was obtained by bubbling a normal culture with $H_2+5\%$ CO_2 for 6 days.

If nitrogen was readmitted aerobically (5% carbon dioxide in air) most series of vegetative cells situated between two heterocysts showed a gradient in phycocyanin fluorescence after 20 h. Intensity was greatest in the cells adjacent to heterocysts and least about halfway between the heterocysts. Normal mature heterocysts do not fluoresce. The most evident fluorescence gradients corresponded to gradients in phycocyanin absorption, so that the results are due to differences in phycocyanin concentration and not in fluorescence yield in different cells. If these gradients are caused by differences in the availability of nitrogen, this experiment shows that in an aerobically grown culture of *Anabaena*, N_2 is fixed exclusively or predominantly in the heterocysts.

If N_2 was readmitted anaerobically (5% CO_2 in N_2), the rate of phycocyanin synthesis was the same but gradients in phycocyanin concentration were rare and far less pronounced than in aerobic cultures. This indicates that in anaerobic conditions vegetative cells also fix nitrogen. It also seems that all cells reduce neotetrazolium in anaerobic cultures. After addition of ammonium phosphate, whether aerobic or anaerobic, no gradients of phycocyanin concentration develop during synthesis of the pigment.

An aerobic culture that was in the process of losing its phycocyanin due to molybdenum deficiency also exhibited concentration gradients. Here heterocysts appeared also in the regions with low phycocyanin content, alternating with heterocysts whose neighbouring cells had a high concentration of phycocyanin. This pattern indicates that these were young heterocysts, differentiated after molybdenum had been exhausted in the medium, and so unable to synthesize nitrogenase. This experiment confirms that the gradients in phycocyanin concentration are due to nitrogen deficiency and that nitrogen is fixed chiefly by the heterocysts. It also seems that molybdenum does not migrate from one cell to another in significant amounts.

Another consequence of the hypothesis is that it should be possible to distinguish nitrogen fixation by vegetative cells and by heterocysts on the basis of their oxygen sensitivity. The reduction of acetylene by anaerobic cultures is strongly, and in part irreversibly, inhibited by oxygen. In aerobic cultures inhibition by oxygen, if any, is completely reversible. In Fig. 1 the oxygen sensitive and oxygen resistant parts of acetylene reduction by the aerobic (*A*) and anaerobic (*B*) nitrogen-starved cultures are plotted as a function of time after readmission of the gas. The dotted line in Fig. 1*A* represents the pattern of acetylene reducing activity during the growth of a normal aerobic culture, which roughly parallels the growth rate. On the first 2 days after nitrogen starvation there is an extra acetylene reduction, which is also resistant to oxygen in the anaerobic culture (Fig. 1*B*). If oxygen resistant nitrogen fixation is located in the heterocysts, this may account for the few and indistinct phycocyanin gradients seen in the anaerobic culture.

Other arguments have been published as evidence that the heterocyst is the site of nitrogen fixation[7]. As Smith and Evans[8] emphasized, the yield of acetylene reduction by isolated heterocysts was too low to permit any direct conclusions. Heterocysts reduce neotetrazolium to formazan crystals after removal of tetrazolium, and acetylene reduction was irreversibly inhibited in filaments in which the heterocysts contained formazan crystals. We found, however, that the formation of microscopically visible formazan crystals, but not the irreversible inhibition of acetylene reduction by neotetrazolium, can be prevented by 2 mM sodium azide during treatment with tetrazolium.

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BOOK REVIEWS

Coral Reefs

Atlantic Reef Corals. (A Handbook of the Common Reef and Shallow Water Corals of Bermuda, the Bahamas, Florida, the West Indies and Brazil.) By F. G. Walton Smith. Pp. xii+164. (University of Miami: Florida, August 1971.) $6.95.

Interest in coral reefs is growing and the republication of this small book, which first appeared in 1948, is welcome. It deals with the coral fauna of the Caribbean and Gulf of Mexico with outlying populations as far north as Bermuda and as far south as the coast of Brazil. Many of the shallow water coral reefs in these areas are among the most readily available in the world, with increasing numbers of marine biologists and interested tourists wading, swimming and diving among the corals.

The shallow water coral fauna of the Atlantic is small enough for it to be largely covered in this small compass with adequate general descriptions and photographs of all common species. Some additions have been made to those originally described but the full list of Atlantic corals, including many from the lowest levels of reef growth, is now becoming considerable. This is largely due to the activities of the late Professor T. F. Goreau and those associated with him in Jamaica. These were to have been monographed by him in collaboration with Professor J. W. Wells of Cornell who will now, it is greatly hoped, proceed with other collaborators.

Where this book fails is in its account of living corals. For example, no mention is made of the mesenterial filaments, those extraordinary structures which wrap round and consume the animal prey within, or sometimes outside, the gastric cavity. The reader is merely told that food is digested by "the mesenteries". The zooxanthellae, endozoic algae the presence of which distinguishes the reef-building or hermatypic corals from the deep or cold water ahermatypic corals, receive bare mention. They are described as "blue green algae" to which they have never been ascribed. It has long been known that they represent vegetative stages of dinoflagellates; they are indeed imprisoned phytoplankton. Their supreme importance in speeding the rate of calcification—the basic difference between hermatypes and ahermatypes—which was experimentally demonstrated by Goreau is not even mentioned.

There is now so very much to tell the general reader about the life of corals that one can only regret that the opportunity has been missed. While I am perhaps flattered to have the reader referred to my *Year on the Great Barrier Reef*, this has now been out of print for a quarter of a century and in any case is completely out of date. However, the reader will get a handy, well organized and illustrated description of all the Atlantic corals that he is likely to encounter.

C. M. Yonge

Forest Radioecology

A Tropical Rain Forest: a Study of Irradiation and Ecology at El Verde, Puerto Rico. Edited by Howard T. Odum and Robert F. Pigeon. Pp. 1,678. (US Atomic Energy Commission: Oak Ridge, Tennessee, 1970.) $10.

Some ten years ago the US Atomic Energy Commission, to meet the pressing need to know more about the effects of radiation on natural ecosystems, embarked on a broad programme of "forest radioecology". The object was to study the damage to forest communities from gamma radiation at intensities comparable with those which might be experienced in a major reactor accident or in the use of nuclear explosives in peace or war. Because different forests would probably not respond to radiation in the same way, it was necessary for studies to be made in more than one type of forest and in several clearly differentiated climatic zones.

The experiments at Brookhaven and elsewhere in the continental United States are well known and have given much useful information on radiation damage in pine and broadleaved forests in a temperate climate. Here, in this huge volume, are the results of investigations carried out since 1963 in evergreen tropical forest in the West Indian island of Puerto Rico. The choice of Puerto Rico had several advantages—it was US territory and easily accessible; the El Verde Experimental Forest, some of which was still in an almost "virgin" condition, was available, and the Puerto Rico Nuclear Center was close at hand. It was a disadvantage that this forest is montane and, being in a hurricane belt and on an island, was in several respects different from the "classical" lowland rain forest of Amazonia or Malaya; conclusions drawn from El Verde may not apply to rain forests elsewhere.

Though the radiation experiment was its *raison d'être*, the El Verde project developed into an extremely wide-ranging study of the rain forest ecosystem as a whole: hardly any aspect or any of its component plant or animal groups was neglected. A vast army of investigators cooperated in the project and ninety-one of them have contributed to this book. The resources of the Atomic Energy Commission made it possible for new methods and a great variety of expensive equipment to be tried out—even to enclosing part of the forest in a giant plastic cylinder 67 feet high and 60 feet in diameter. The 111 chapters in which the results are recorded vary greatly in importance: some are mere progress reports but others add notably to knowledge of rain forest ecology.

To put the Puerto Rico studies in perspective, work was also carried out in Dominica (which has a forest dominated by *Dacryodes excelsa* very similar to that at El Verde), at Panama and elsewhere.

To review critically the contents of a book such as this is hardly possible. Though the themes of energy utilization and the mineral cycle run throughout the book and Dr Odum in a final chapter entitled "An Emerging View of the Ecological System at El Verde" makes a courageous attempt to integrate the results, the appreciation of such a mountain of information requires time and experience beyond the resources of a single individual.

It may indeed be doubted whether the radiation experiment itself, important as was its aim, was the project's chief accomplishment. For practical reasons it could not be replicated and, because the treatment was not identical, it is not possible to make exact comparisons with Brookhaven and other sites. The results are not clear cut, though they seem to indicate that the tropical forest is less radiation-sensitive than that at Brookhaven.

On the other hand, the new insights into the rain forest as a functioning ecosystem are a great gain and will be studied with profit for a long time to come. Here for the first time can be found quantitative data on such subjects as the holes made in leaves by herbivorous insects, the half-life of leaves (four to nine months in most species) and a mass of interesting information about the roots and buttresses of tropical trees. Particularly fascinating are Odum's chapter on rain forest structure and mineral cycling homeostasis and such sidelights as the evidence for the part played by epiphyllae in the mineral cycle. A first attempt has been made to determine the age of a tropical tree by radiocarbon dating of the heartwood (370 ± 150 years in *Dacryodes excelsa* in Dominica).

If this book, in the hackneyed phrase, is chiefly a mine of information, one could perhaps ask for the miner's task to be made easier. Was it necessary to bind the 1,678 pages into a single volume or even to bind them at all? At $10 the book is a good buy, but a collection of separate articles would have been more comfortable to read than a volume measuring 28×22×6.5 cm and weighing nearly 5 kg. Reference would be easier if the number of the chapter and the author's name had been put at the head of each page.

Though the organization of the book is unsatisfactory, one can be grateful for the new knowledge it contains. No rain forest has ever been studied so intensively as El Verde. It is a pity that it requires the threat of nuclear disaster to make such a project possible.

P. W. RICHARDS

Excitable Cells

The Physiology of Excitable Cells. By D. J. Aidley. Pp. ix+468. (Cambridge University: London, June 1971.) £5.80; $15.

PERHAPS every scientist considers that the recent history of his own discipline is the best demonstration of the scientific method in operation. That many neurophysiologists are of this opinion is understandable after reading D. J. Aidley's book, *The Physiology of Excitable Cells,* for this is a collection of elegant and intellectually satisfying experiments and analyses which, taken as a whole, contribute greatly towards an understanding of the fundamental workings of the nervous system.

After a brief introduction which deals with the concepts and techniques particular to the electrophysiologist, the book can be divided into three principal sections. The first concerns the neurone and the structure and electrochemistry of the cell membrane, both in the resting condition and during the propagation of the action potential. This is followed by a consideration of the neuromuscular junction and the physiology and pharmacology of synaptic transmission. The second section develops the subject of muscular contraction, building up from the essential structure of the myofilament and the coupling of the processes of excitation and contraction, to a study of the activity of entire muscles. The third section begins with a statement of the general principles that apply to the functioning of sensory receptors and the principles are then illustrated by reference to special sensory systems. These systems are the acoustics-lateralis system of vertebrates, mammalian muscle spindles, insect chemoreceptors, electroreceptors and the vertebrate eye.

The scope of the author's approach is impressive and has certainly involved the unenviable task of assimilating a great variety and depth of source materials. The result is a text written in an economical style which develops the various themes in a logical and, for the most part, highly coherent way. The many mathematical arguments involved are well presented and adequately explained, the value of hypotheses is carefully weighed and the evidence for them is discussed in a good critical manner. In addition a genuine attempt has been made to develop a comparative approach so that various classical preparations, such as the squid giant axon, are placed in their proper comparative perspective and the inclusion of chapters on the electrical properties of glial cells and the physiology of the electric organs of fish enhances the impression of a well rounded account.

One small criticism is that the section on sense organs would not suffer from some expansion, nevertheless, this book more than fulfils its intention of being a course book for undergraduate students of neurophysiology and its comprehensive nature and critical style place it in favourable comparison with respect to other, and usually more restricted, works on the subject.

JOHN A. PATTERSON

DMSO Re-evaluated

Dimethyl Sulfoxide. Vol. 1: Basic Concepts of DMSO. By Stanley W. Jacob, Edward E. Rosenbaum and Don C. Wood. Pp. xv+479. (Dekker: New York, February 1971.) $27.50; £13.10.

HERALDED as a new "wonder-drug" in 1964 and then condemned as dangerously toxic in the following year, dimethyl sulphoxide (DMSO) has been one of the most controversial chemicals of modern times. Although first prepared nearly a century earlier by Alexander Saytzeff, it was Stanley Jacob's and Robert Herschler's discovery of its unique tissue penetrating powers and its diverse pharmacological activities which led to the widespread interest in DMSO, particularly for its use as a solvent vehicle which enhanced the percutaneous absorption of drugs and for the many potential clinical applications in human and veterinary medicine and in agriculture. But reports of toxic effects to the lens of the eye in experimental animals (which have not been reproduced in man or primates) led the US Food and Drug Administration to terminate promptly the clinical investigations on the drug which were just getting under way. Many scientists, particularly Drs Stanley Jacob and Chauncey Leake in the United States and Dr Gerhard Ludahn in Europe, held faith with the new drug and subsequent work has indeed shown that the early reports of toxicity may have been exaggerated and the cessation of clinical studies was perhaps unwarranted.

Some five or more years later, the initial over-enthusiastic acclaim of its potential as a drug and the following hasty condemnation have now given way to a more reasoned attitude with critical scientific evaluation replacing emotional subjective opinion, and the possible clinical uses of this interesting compound are being re-examined. The time was therefore most opportune for the publication of this evidence in its entirety and this is the stated intention of the editors of this encyclopaedic monograph on DMSO. In this first volume Stanley Jacob and his colleagues Edward Rosenbaum and Don C. Wood have brought together their own extensive published work on the subject and, along with that of many collaborators, have produced an impressive work of reference which covers the chemistry, biochemistry, pharmacology and toxicology of DMSO together with its radioprotective and cryoprotective properties and its uses in enzymology, microbiology, immunology, dermatology and veterinary medicine. This was no small task, for the published literature on DMSO is extensive, as may be adjudged from the number of references cited, which is well over two thousand. Somewhat regrettably, however, there is duplication of many of these in the last chapter entitled "DMSO Bibliography" which, for no stated reason, is confined to cryobiology, chemistry and pharmacology.

Nevertheless, this is an outstanding work of dedication by scientists and clinicians who believe in the future of DMSO. It is excellently presented and lucidly written and it will form the standard work of reference of the subject for biomedical scientists of all disciplines. The second volume of this monograph will contain reviews of the clinical studies on DMSO and it is to be hoped will present some of the most vital evidence of this controversy and thus complete the case for the reinstatement of DMSO as a useful agent in clinical medicine.

DENNIS V. PARKE

Camera in the Gut

The Digestive System. By P. G. Toner, K. C. Carr and G. M. Wyburn. Pp. x+303. (Butterworth: London, July 1971.) £10.

THIS book presents a timely synthesis of form and function in the alimentary tract and should have a wide appeal not only to basic scientists but also to gastroenterologists who seek a cellular background to their speciality. Written by a pathologist and two anatomists, the book surveys the normal cellular anatomy of much of the digestive system at the electron microscope level. Individual organs are not considered as single entities ; the emphasis is on the various types of epithelial cell from the oesophagus downwards. There is a section on mucosal architecture and cell renewal in the small intestine illustrated by optical and scanning electron microscopy, the latter providing a dramatic three dimensional surface view of the pattern of crypts and villi. Other regions of the tract are unfortunately not shown in this way. Salivary gland cells are considered, together with those of the liver, gall bladder (but not the bile duct), pancreas and Brunner's glands, and there is a final short chapter on non-epithelial components.

There are some 200 illustrations depicting both human and laboratory animal material. The prints are of a kind that most photographers would regard as "contrasty", but this is not meant as an adverse criticism, for they are of a generally high quality (the worst is the very first!). The legends are fully explanatory and their layout on the text page is pleasing. The text itself makes easy reading and the description of each cell type leads up to the all-important point—the correlation between structure and function, with suitable comment on those areas where current knowledge is sparse. There is a good summary of the endocrine cell problem as it existed at the time of going to press, but almost every month now brings new information on the cells that produce gastrin, secretin and other intestinal hormones, and no book can capture the latest word on this subject at present. There are useful reference lists, including an up-to-date addendum. An occasional typographical error has escaped the proof readers.

This volume is a significant contribution to the literature of gastroenterology and it is hoped that one of its effects will be to stimulate collaboration between clinician and basic scientist. Such rapport can bring nothing but good—provided that each recognizes the problems and limitations of the other in their respective fields of investigation. A book of this kind makes electron microscopy look all so easy, and many clinicians especially do not appreciate the amount of time and effort that has to be expended to obtain one good photomicrograph, let alone two hundred. R. M. H. McMinn

Primary Battery

The Primary Battery. Vol. 1. By George W. Heise and N. Corey Cahoon. (The Electrochemical Society Series.) Pp. xvi+500. (Wiley: New York and London, April 1971.) £12.

It is more than twenty years since G. W. Vinal's well known book on primary batteries was published. In this time a commercial demand has been established for MnO_2/KOH/Zn and HgO/KOH/Zn batteries, and AgO,Ag_2O/KOH/Zn batteries have proved important for special high power density applications. Fuel cells have caught the public imagination for their role in space exploration and their potentiality in electric cars. These batteries, the Leclanché battery and other novel systems have benefited from considerable funds supplied by governments and private industry over two decades of intense activity and electrochemical awareness. A new book is clearly overdue. Indeed, almost a generation of battery technologists has matured and deplored the absence of a modern reference work to ease the task of assimilating existing knowledge.

Although the book under review is only the first of two volumes, the authority and care taken in compilation make clear that the work will be one of importance. The criticisms that follow are not intended to detract from this overall conclusion.

The historical introduction is by George W. Heise and the periods up to 1880 in particular are well done with events shown as a logical train rather than as a series of random happenings. It is regrettable that the period 1880–1920 which contains the origins of the important Leclanché dry cell is only dealt with sparsely. Heise himself must be uniquely placed to review this important era.

The chapter on fundamental aspects by Ernest B. Yeager and Eugene P. Schwartz with appendices comprises 22 per cent of the book. It is carefully worded, helpfully slanted in directions of battery interest and written to be understood. Apart from useful experimental advice on techniques, circuits and equipment, much of the content is available elsewhere in standard electrochemical texts. The electrode-solution interface is treated in depth and, while this is the heart of the battery process, fundamental instruction is also required on electrolytes, the solid state, separators, mixing, mixtures, particle technology and porosity, which are not considered. There seems little reason to include twelve pages of standard potentials derived from well known reference works, particularly since many are not relevant to primary batteries and those which are are given in another form in a further appendix. In the further appendix the data for the Leclanché cell are of doubtful value since Mn_2O_3 is represented rather than MnOOH.

The next six chapters, "Primary Cells with Caustic Alkali Electrolyte", "The Alkaline Copper Oxide: Zinc Cell", "Zinc: Oxygen Cells with Alkaline Electrolyte" all by Erwin A. Schumacher, "The Mercuric Oxide: Zinc Cell" by Samuel Ruben, "The Silver Oxide: Zinc System" by Thedford P. Dirkse and "The Alkaline Manganese Dioxide: Zinc System" by N. Corey Cahoon and Harry W. Holland, are the *raison d'être* for this volume. These batteries are all made industrially for profit and fulfil a useful function in society. The treatments are adequate but except for the chapter on zinc: oxygen cells one is a little disappointed in their brevity. Ruben, for example, modestly dismisses his important invention in around 3,000 words. Something has gone seriously awry with tables 3.1 (page 171) and 3.2 (page 176). Clarification is needed to avoid any impression that Mn_3O_4 is involved in the initial open circuit voltage of MnO_2/KOH/Zn cells (page 239) or that the cited degrees of on-load voltage stability for HgO/KOH/Zn cells are achieved if MnO_2 is incorporated into the cathodes (pages 213, 214).

The final four chapters attain a very high standard. In "Fuel and Continuous Feed Cells" Ralph Roberts has summarized an immense amount of development effort in a concise and balanced account. Advances are shown without losing sight of the real objectives and the very considerable problems that still remain. "Low Temperature Non-aqueous Cells" by John M. Freund and William C. Spindler is instructive and readable. "Semidry and Solid-Electrolyte Batteries" by John N. Mrgudich and Demetrios V. Louzos is a stimulating chapter which gathers together for the first time much information in a logical and digestible form. Finally, Walter J. Hamer has built on the solid foundations laid in Vinal's book to produce a discussion of "Standard Cells" and related aspects that is excellent in all respects. F. L. Tye

Biochemistry of Babies

The Biochemistry of Development. Edited by Phillip Benson. Pp. v+273. (William Heinemann Medical Books: London; J. B. Lippincott: Philadelphia, 1971.) £3.25.

There is a type of publication, with which all biologists are familiar, in which a handful of indifferent papers are mixed with a little elementary biochemistry, inadequately edited, given a grandiloquent title and a fancy cover, graced with a blurb or preface which explains that they are essential reading for all practising frothblowers, published at an exorbitant price and sold at a handsome profit to institutional libraries. In spite of some striking superficial resemblances Dr Benson's book does not belong to this depressing category. Behind its general and rather misleading title it is a collection of essays on the narrow but important and exciting theme of the biochemistry of the foetus and the newborn mammal. Although the chapters are numbered as though they formed part of a continuous exposition they are quite independent of one another. They deal, at varying levels of specialization, with a wide variety of topics. The core of the book is formed by five chapters which together form a fairly coherent account of the general biochemistry of the foetus, of the biochemical changes which accompany its development, and of the dramatic biochemical readjustments which take place when it is born. The treatment is rather uneven. The lipid chapter, for example, includes a higher proportion of elementary and general material than the others. The chapter on urea biosynthesis, at the other extreme, seems to be based largely on the author's own experimental results. Dr Benson's own chapter starts with a review of the regulation of genetic expression but incorporates a quite detailed account (with numerous figures) of his own experiments. The remaining chapters deal with mere isolated topics: the regulation of foetal liver development; the intrauterine diagnosis of inherited disease; foetal haemoglobin; the autacoids; and polymorphism in human proteins.

Considered as a collection of biochemical essays the book has substantial merits. The topics with which it deals are intrinsically interesting and not perhaps sufficiently well known to biochemists. Though the contributors vary so much in their approach, the quality of their contributions is generally high. Their variety itself is an advantage to the casual reader. It is perhaps too strictly biochemical in its approach and too full of biochemical technicalities to be readily intelligible to most of the paediatricians and obstetricians to whom it is apparently addressed. But almost any intelligent student of biochemistry is likely to read at least some of the chapters with interest and enjoyment. For a work addressed to a fairly specialized audience and therefore with limited circulation, its price is surprisingly reasonable.

R. Y. THOMSON

Soviet Rocketry

Soviet Rocketry: The First Decade of Achievement. By Michael Stoiko. Pp. xi+272. (David and Charles: Newton Abbot, August 1971.) £3.25.

IT would, perhaps, be better to call this book something like "A Kremlinologist's Notes and Thoughts on Soviet Rocketry". The first chapter (pages 1–16) gives a sketchy outline of the early history of rocketry in the world, but contains several factual inaccuracies. The second chapter (pages 17–24) is called "Tsiolkovsky's Legacy", but no analysis of his historic contributions appears. On page 18 we meet the old acquaintances: "he mastered mathematics *first* and *then* physics", and "in 1881 he began his first serious scientific research in *three areas*—all-metal dirigibles, airplanes and rockets".

Tsiolkovsky wrote his famous letter not to the Central Committee of the Communist Party (page 24), which is a post-cult-of-personality formulation, but to the great teacher and leader I. V. Stalin, whose address was the Central Committee.

On page 26 we read that "Tsiolkovsky's chief contribution lay in his conclusion that the only possible means of flight in space must be based on the reaction principle. . . ." I think that this is a somewhat untidy formulation since (1) the reaction principle was known to and had been used by man centuries before Tsiolkovsky was born; (2) Tsiolkovsky's collected works, especially his *Album of Space Travel*, show that the range of his contributions to rocketry and space travel was very much wider than the reaction principle; permanent orbital stations, regeneration of biological waste in space, energy problems in free space, space walk, space plants—all these and many other subjects were studied by him quite rigorously.

Chart 1 on page 32 ("Evolution of Soviet Rocket Societies") contains factual mistakes (the positions of Tsander, Korolyev and Kostikov, GIRDs throughout the USSR). The statement that after the formation of the Zhukovsky Academy "at least fifteen comparable academies of astronautics have been built" (page 30) is wrong; one can guess that the author intended to say "fifteen *military* academies", which is a different thing. Statements such as "during the years 1928–30 *numerous* rocket conferences were held" in the USSR, "GIRD became *national* in scale with branches in *major cities*" (page 47) and a "Rocket Research and Development Centre" (page 47) was established in 1932 at 19 Sadovo-Spasskaya Street are obvious exaggerations conflicting with facts. And certain remarks about M. K. Tikhonravov and V. P. Glushko (page 62) do not hold water.

Chapter 6 ("Prelude to Sputnik") describes rocket work in Germany and the Soviet Union up to August 1957. The rest of the book deals with the now well known Soviet space achievements and attempts to outline their organizational skeleton; the principal facts are described accurately, the illustrations are good, but up to thirty inaccuracies and mistakes of varying importance have been noticed.

The gloomy warnings by Richard Nixon (then Vice-President) on October 16, 1957 (that Sputnik 1 was "a grim and timely reminder" to the United States) and by Vice-Admiral Hyman G. Rickover in 1961 (that "the United States and Russia are not engaged in a popularity contest but in a grim technological race") seem to be irrelevant and unnecessary. The somewhat *à vol d'oiseau* foreword by Patrick Moore confuses Russia with USSR and vice versa.

No sources of information are given anywhere, but a bibliography is available at the end of the book.

G. A. TOKATY

Eastern Libraries

Libraries in the East: An International Comparative Study. By George Chandler. Pp. 214. (Seminar: London and New York, 1971.) £2.50.

INFORMATION about the development of libraries and librarianship in the East is scattered throughout Unesco and other report literature, or appears in short articles in the periodicals of the countries concerned. Thus it is difficult to obtain a complete picture and especially to study progress on anything like comparable terms. The present book aims to survey the recommendations which have been made at Unesco seminars on the development of library services in the East and to compare the advances in eight Eastern countries (the Lebanon, Egypt, Iran, Pakistan, India, Thailand, Hong Kong, and Japan) as seen at first hand during a tour by the author as president of the International Association of Metropolitan City Librarians (INTAMEL). The countries are taken in turn and considered under such headings as the structure of the library services, library associations, schools of librarianship, national libraries, documentation centres, and, where appropriate, public, special and academic libraries.

Inevitably coverage is variable because it is limited almost entirely to institutions visited on the tour made in 1970. It is admitted that, where certain libraries are selected for detailed consideration, though the intention was to reflect general problems for the East as a whole, choice in the last analysis was personal or even accidental, depending on the information provided by the librarians of the libraries visited. Nevertheless, we are appreciably further forward in knowledge of Eastern libraries and indebted to Dr Chandler for presenting the information gained on his tour in the constructive framework of a comparative study. Many readers will wish that personal impressions of each country's library development were given much more space and prominence. These "conclusions", which are limited to six or seven lines of text, do not appear for every country. An appendix provides a select bibliography of Eastern libraries, covering the period 1950–1970, and a second appendix reprints a survey of library service in Asia prepared for Unesco in 1967.

WILFRED ASHWORTH

CORRESPONDENCE

Preserving Rare Breeds

SIR,—I was interested to read your report, "Keeping Fossils Alive"[1], of a conference on "rare breed survival" which was held on October 15. This correctly refers to the fact that rare breeds of cattle, sheep and poultry had been kept as a "gene bank" at Whipsnade, but is wrong in saying that the animals "had to be dispersed when the Zoological Society of London needed the space".

The story is as follows. On a decision taken by the Society's council, small flocks and herds of rare native domesticated breeds were collected and established at Whipsnade in 1961 with the object of preserving them, not merely as historic remnants, but as material for study by geneticists, physiologists and other scientists. An offer to put the animals at the disposal of *bona fide* investigators and to collaborate in their research projects was made in your journal in 1964[2]. A useful study of the blood groups of sheep was carried out by Tucker[3]; otherwise the response to our offer was disappointing, and we failed either to stimulate interest or to obtain financial support for the appointment of scientists to our own staff to study these animals.

After exchanges with other scientific bodies, and following much deliberation by its scientific committees, the council of the Society was advised that greater use might be made of these valuable stocks if they were transferred to agricultural institutions where they would attract the interest of students, and where better facilities for rearing the young would be available.

Accordingly, in 1968, flocks of three breeds of sheep were transferred to Professor Bowman at the School of Agriculture, University of Reading. Arrangements were made with Mr Christopher Dadd, Director of the National Agricultural Centre, for the transfer of the remaining four breeds of sheep to Stoneleigh Park, Kenilworth, where they have now attracted considerable public interest. In 1970, the NAC was also presented with surplus animals from the Zoological Society's herd of Chartley Cattle at Whipsnade.

What I should like to correct is the statement that the Society dispersed the gene bank it had established on its own initiative because "space was needed". The animals were sent to institutions where it was hoped they would attract more interest than they had done at Whipsnade and where they would consequently be of greater value to agricultural science.

Yours faithfully,

LORD ZUCKERMAN

Secretary

Zoological Society of London,
Regent's Park, London NW1 4RY

[1] *Nature*, **233**, 587 (1971).
[2] Rowlands, I. W., *Nature*, **200**, 131 (1964).
[3] Tucker, E. M., *Nature*, **216**, 684 (1967).

Obituary

Sir Ernest Marsden

[Photo by Walter Bird

ERNEST MARSDEN, who died at the end of last year, was born at Rishton, Lancashire, on February 19, 1889. His mother had a hardware shop, selling cooking utensils, nails and similar goods. Ernest was one of four sons, and helped in the shop from time to time. In the school holidays he used to go to his aunt's at Blackpool, where he helped with washing up, cleaning knives and peeling potatoes, to earn pocket money. After attending the local school at Rishton, where he had already exhibited ability, he was sent to the Grammar School at Blackburn.

In 1906, when he was eighteen, he enrolled in the department of physics at Manchester University. Schuster and Petavel were still professors, and in 1908 he began research in atmospheric physics under Petavel. With the arrival of Rutherford in that year he changed to atomic physics. In 1909 Rutherford assigned him to assist Geiger in research on the scattering of α-particles. Before he had graduated, and before he was twenty years old, Marsden collaborated in the crucial experiment from which Rutherford established the nuclear structure of the atom. Five years later, pursuing Rutherford's general plan of exploring the collision of swift particles with matter, Marsden observed that when α-particles were projected into hydrogen, a few of the hydrogen nuclei were knocked forward far beyond the range of the α-particles.

His brilliant work and general capabilities caused Rutherford to recommend him for the most important chair of physics in his native land, at Victoria University College, Wellington, New Zealand. Marsden was appointed at the age of twenty-five. Rutherford asked him whether he would mind his taking over the experiments on the impact of α-particles on hydrogen gas. In the following two years, during the First World War, Rutherford continued these experiments; by 1917 he had evidence that protons were being ejected from atoms—that the artificial disintegration of the atom had been achieved. Thus Marsden contributed to two of the most significant experiments in modern physics. In the early work on large-angle scattering, Marsden perceived that his observations implied that the atom might have a nuclear structure. But he was too young to have the confidence, or to have acquired the scientific knowledge and maturity, to put the idea forward and prove that it was true. The full force of Rutherford's genius was needed to do that.

In stature Marsden was short and stocky. He had the physique and liveliness of the Lancashire man of his period, and he spoke with the local accent. He was a Lancashire lad, generally referred to as "Ernie" behind his back, a typical descendant of the people who had done so much to create the industrial revolution, with their combination of intelligence, ingenuity and enterprising common-sense. Like his great master, Rutherford, he had a feeling for people, and inspired them by his genuine interest in their concerns, however bluff his comments might be.

Shortly after arriving in New Zealand in 1915, Marsden was commissioned in the New Zealand Engineers. He was seconded to the 1st NZ Expeditionary Force, and embarked for Europe in 1916. He served with distinction in the development and operation of sound-ranging, being twice mentioned in dispatches, and was awarded the Military Cross.

After demobilization in 1919 he returned to his chair. He taught the varied collection of Wellington students with a natural enthusiasm and love of his subject, and persuaded the authorities to build a handsome new laboratory.

Almost as soon as he had launched these developments in physics his human as well as his scientific qualities attracted the attention of the Government. In 1922 he was appointed Deputy Director of Education in New Zealand. He became involved especially in matters connected with science. The need for the systematic organization of scientific and industrial research had become patent, so, in 1926, the New Zealand Department of Scientific and Industrial Research was set up, with Marsden as its first Secretary. He organized the first industrial research associations, promoting research over a wide range of sciences including physics, chemistry, geology, and food and agriculture problems. He inspired the harnessing of thermal energy from the ground, as well as the investigation of the causes of cracks in cheese, poor spreadability in butter, the control of weeds, poor baking quality in wheat, deterioration in frozen meat and chilled fruit cargoes to Britain. During the depression of 1933–39 he stimulated the application of geophysics to the development of New Zealand mineral resources, and new possibilities for the utilization of plant and animal products. Among the successful subjects of research were the treatment of bush sickness, the quality of wheats, and the transport of beef.

In the Second World War Marsden had the leading part in adapting and developing New Zealand's scientific resources to meet the situation. He expanded the Dominion Physical Laboratory, and promoted research in submarine detection. The Radar Development Laboratory which he established supplied US forces in the Pacific with 110 radar sets before these could be provided from home American sources. He originated the Defence Science Corps.

Marsden naturally became the chief representative of New Zealand science on the national and international scene. He became a familiar and much respected figure as Scientific Liaison Officer in London, both in military and civil matters. In 1947 he was appointed New Zealand Government Scientific Adviser in London. As such, he became the chief New Zealand representative in the post-war United Nations scientific developments.

Marsden retired in 1954, but continued an active scientific life up to his seventy-seventh year. He became particularly interested in bioradiation and cancer research. He believed that radioactivity inhaled from tobacco smoke was a cause of lung cancer, the radioactivity being derived from the soil in which the tobacco had been grown.

Marsden was elected a Fellow of the Royal Society in 1946, and President of the Royal Society of New Zealand in 1947. He was knighted in 1958. He received many scientific awards and distinctions, but one which he very specially valued was his presidency of the Rutherford Jubilee International Conference at Manchester in 1961, in celebration of the fiftieth anniversary of the demonstration of the nuclear theory of the atom.

In 1913 Marsden married Margaret Sutcliffe. They had a son and a daughter, both of whom are in New Zealand. He married Joyce Winifred Chote in 1958. He died on December 14, 1970.

Errata

The review in last week's *Nature* by Lancelot Law Whyte "Science and Synthesis" (*Nature*, **234**, 159; 1971) was unfortunately published under the wrong bibliography. This should have been as follows: *Science and Synthesis.* (An International Colloquium organized by Unesco on the Tenth Anniversary of the Death of Albert Einstein and Teilhard de Chardin.) Pp. vii + 206. (Springer: Berlin and New York, 1971.) 38.50 DM; $10.50.

In the article by E. A. Barnard, J. Wiekowski and T. H. Chiu on page 207 of this issue, the manuscript was received on June 23 and was not revised as stated.

International Meetings

December 7, **The Determination of Non Metals by Atomic Spectroscopy,** London (Society for Analytical Chemistry, 9–10 Savile Row, London W1X 1AF).

December 14, **Financial Control of R and D,** London (Science Policy Foundation, Benjamin Franklin House, 36 Craven Street, London WC2N 5NG).

December 15, **Public Participation in Highway Planning,** London (Institute of Civil Engineers, Great George Street, London SW1).

December 17, **Applications of Vibrational Spectroscopy to High Polymers,** London (Dr W. O. George, School of Chemical Science and Technology, Kingston Polytechnic, Penrhyn Road, Kingston upon Thames, Surrey).

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Smoke But No Fire So Far

LORD ROTHSCHILD'S prescription for the future organization of civil scientific research in Britain seems to have excited so far only mild and even polite interest. The newspapers have reported without much comment the suggestion which is the nub of the Rothschild report (see *Nature*, **234**, 169 ; 1971) that applied research carried out by the research councils should in future be paid for out of the budgets of the government departments most likely to benefit from the results, but there has been no sign so far of how the proposal will be allowed to influence the future pattern of expenditure. On balance, the research councils are likely to dig in their heels and resist the application of the principle, but some of their determination may have been undermined by one of the few public statements so far, that in which Sir Harold Himsworth, director of the Medical Research Council until two years ago, told readers of *The Times* that he, for one, was opposed to Rothschild. After all, there comes a point when excessively ardent defenders of an entrenched position make it impossible for others to adopt more moderate points of view. And, this is the flaw, Sir Harold Himsworth has chosen to resist Rothschild on the grounds that the Haldane doctrine, first spelled out half a century ago, is still appropriate to the management of British public expenditure on scientific research. The truth is, as some of Rothschild's sternest critics will agree, that the Haldane principle has become an archaic survival from the past.

What is the issue ? Sir Harold says that the effect of what Lord Rothschild has proposed would be to transfer to government departments the initiative for developing new lines of research in such fields—where the Medical Research Council is concerned—as clinical and para-clinical medicine. He goes on to say that "departmental policy can only be based on knowledge that exists at the time it is framed" and that "at any time research may show that this is faulty and that, accordingly, official policy is mistaken". In short, Sir Harold says that government departments have a vested interest to steer clear of research for fear of being shown up and that they are especially likely to avoid "those parts of their work that are most relevant to current issues". It is not necessary to believe in the infallibility of government to know that this argument is and should become invalid. After all, the days are gone when research was entirely a novelty in government work. Although it may have been sensible in the early decades of the century to fear that government departments would so entirely misunderstand the function and potential value of scientific research that they would discount it altogether, time has shown even the most iconoclastic departments that there can be practical value in the work that scientists do. Not merely in Britain but elsewhere, government departments are anxiously waiting for such diverse benefits as improved methods of air traffic control, better understanding of the ways in which impoverished families become poor and the ways in which military technology may be transformed by scientific developments. And although scientific research is bound in the long run to be subversive in the sense that it will introduce people (civil servants included) to notions which have previously not crossed their minds, there is very little evidence that the research councils in the past fifty years have been successful at confronting governments with awkward scientific appraisals of their immediate actions. On the contrary, for all Sir Harold Himsworth's protestations, the research councils have been exceedingly uncontentious in their dealings with government and in their handling of issues of public importance which might be illuminated by scientific research (and which are usually ignored). In short, the full-blooded defence of the Haldane principle that there should be a separation between publicly supported research and the government departments most likely to be affected is false.

Is it nevertheless possible that research councils separate from government departments may be more imaginative spurs to innovation ? This is one of Sir Harold Himsworth's points. So far as performance is concerned, the record is patchy. The Medical Research Council itself, Sir Harold's old bailiwick, has been exceedingly bold in its determined support of molecular biology, but much less interested in more humdrum matters such as the efficient use of hospitals for the treatment of patients—the operational research of applied medicine, so to speak. The Agricultural Research Council has supported some splendid basic research in universities and in its own research units, but has made its reputation on practical developments of immediate value to British agriculture. So far, the Natural Environment Research Council has not been able to make a significant mark on the conduct of public affairs, partly through youth and partly because it is an exceedingly amorphous and even artificial entity. In the past few years, the Science Research Council has had a profound and valuable influence on the development of policy in higher education, while the Social Science Research Council is doing splendid work in the improvement of the standard of social science in Britain, but the research councils immediately threatened, if that is the word, by the Rothschild proposals could probably have been every bit as imaginative as they have been if it had been necessary for them to win support for individual projects from sponsoring departments.

So why not adopt the Rothschild recipe in its entirety? The difficulty, of course, is not a matter of principle but of practice. For every objection to the Rothschild recipe, there is a countervailing argument in its favour. And who will deny that it would be extremely valuable for everybody if British government departments were required by circumstances to develop close relationships with scientific research laboratories? As things stand, however, nobody can be sure that the particular machinery described in the Rothschild report, which requires that government departments should develop ways of formulating their needs of scientific research, will function as efficiently as they might. This is why the first response should be not a decision of principle between the conflicting proposals of Sir Frederick Dainton and Lord Rothschild but a carefully calculated experiment to demonstrate the effectiveness or otherwise of the proposed links between the departments and the research councils. The best place to start is with the Agricultural Research Council. An obvious field of research is plant breeding, where both the Ministry of Agriculture, Fisheries and Food and the Agricultural Research Council are at present spending money. The object should be not so much to save on expenditure—only ten per cent of the Agricultural Research Council's budget would be affected—but to see whether a changeover from the present system to one in which the interaction between the research council and the government departments could be organized efficiently.

But who would ever be in a position to tell ? One of the gaps in Lord Rothschild's argument is that his framework for the future pattern of publicly supported research in Britain makes no provision for the involvement of members of the public except as taxpayers. It may be argued in his defence that the research councils (with the Social Science Research Council and, to a lesser extent, the Science Research Council notable exceptions) have been culpably over-secretive about the planning of their work. Too often they have declined to justify in public even such important aspects of public policy as the setting up of research units separate from (if linked with) universities. Too often they have declined to give serious thought to defining their strategy. One of the dangers of the Rothschild recipe is that it will make it easier for the public servants directly concerned to conceal the kind of arguments by means of which amicable relations are to be established between customers and contractors. If anything, this is a time when there should be a move in the opposite direction, towards less secrecy and confidentiality. What this implies is a need somehow to devise ways of allowing outsiders to know more about the relations between the research councils and the government departments with which they are primarily concerned. Those who wish to see the research councils retain some semblance of independence under the new regime would be well advised to worry about this point.

Keeping the Computer Flag Flying

NATIONAL pride, once satisfied by the creation of a national air line or a television network, now tends to centre on pieces of advanced technology. This is the spirit in which the House of Commons Select Committee on Science and Technology seems to have approached the question of how to stimulate the British computer industry, so that it is something of a relief that its report on the subject, published two weeks ago (see *Nature*, **234**, 117 ; 1971), contains good sense as well as flag-waving. The committee is certainly on sure ground when it says that the most effective way of using government funds to promote the health of one sector of industry is to spend money on research and development, not on the purchase of products at uncompetitive prices. There is less to be said for the committee's proposals for the administration of government policy in present circumstances. And it is painfully apparent that the committee has not been able to trim its arguments to suit the prospect of British entry into the European Communities. Where does flag-waving stop and international cooperation begin?

The Select Committee's blind sense of patriotism is most clearly expressed by the way in which it overlooks the question whether Britain might not be better off without an industry for manufacturing computer hardware. Instead, the committee arrives almost without argument at the conclusion that "a strong independent industry for the supply of equipment and services should be fostered within the United Kingdom". (In this connexion, "independent" implies independence from the several United States companies already established in Britain.) Unfortunately, this proposition is not nearly as self-evident to outsiders as it seems to have been to members of the committee. For a country such as Britain, computer technology can bring two kinds of benefits. First, there are the economies in business and government operation which the efficient use of computing machinery can bring. Second, there are the still less tangible benefits to be won from the existence of commercially successful and entirely indigenous industry. In an ideal world, the Select Committee would have set about the difficult but important task of striking a balance between these partially opposing considerations. It is a great misfortune that the occasion has been allowed to slip.

What might have been said ? In spite of the wave of disillusion which has recently afflicted potential purchasers of computers, British investment in computing equipment —software as well as hardware—has in the past few years been running at about five per cent of industrial capital investment. That is a measure both of the importance of computing machinery and of the need that commercial and public organizations should be able to buy what suits them at prices which are as low as possible. Plainly it is an important part of the government's responsibility to foster use of the new technology, wherever the equipment may have been manufactured. The important question is to know how much energy to devote to that good cause and how much to divert to the building up of a computer industry with roots in national soil.

The case for supporting a strictly British computer industry is not self-evident, to say the best of it. For several years, the chief instrument of the government's policy has been the company now known as International Computers Limited, with a turnover of £130 million in 1970, forty per cent of it abroad. Although the government has in the past three years provided £13 million of research and development money (in return for five per cent of the equity), the company is smaller than the British subsidiary of IBM, which had sales of £170 million in 1970. In spite of the preference which ICL has been given in bidding for government contracts, which has for practical purposes shut out the subsidiaries of American companies, imports of computing machinery have grown quickly. ICL's performance overseas has been creditable, but there is enough internal evidence about the British market for computing machinery to suggest that the products of other manufacturers have important competitive advantages. It is true that this balance may easily be changed by the performance of the new range of time-sharing computers on which ICL has been working, but that remains a hope and not a promise. In the meantime, it must be a serious question whether ICL will be able to deliver all the goods which its potential customers will be looking for in the years ahead.

The Select Committee might also have asked itself what would happen if ICL were to vanish from the scene. The obvious danger that skill in the manufacturing of computers would be lost to Britain is unreal, for most of the 20,000 people now working in the computer industry are employed by other companies. In any case, skill resides increasingly in the software houses. The fear that the present adverse balance of payments on computers might deteriorate still further would also be countered, in part at least, by the willingness of the companies with headquarters overseas to fight for a larger share of what would be a richer honey-pot if government preference for the single British manufacturer were abolished. In this calculation, the difference between the amount of profit accruing to British-owned companies and to the British subsidiaries of foreign companies is of course entirely unimportant. What does matter is the possibility that a strictly British enterprise might provide a better foundation for exploiting by-products of computer manufacture or might be a more efficient trojan horse for carrying British manufacturers within the walls of the European Communities. The Select Committee left both these arguments strictly to one side.

What are the long-term benefits of a British computing industry ? And how should the British Government exploit them ? Quite sensibly, the Select Committee lays down the principle that government subvention should consist of support for research and development, not protection against the harsh winds of competition, but it promptly goes back on itself with the proposal that there should be a Computer Purchasing Board responsible for coordinating government procurement and with instructions to give preference to "suppliers where the controlling interest is held by UK nationals". In the first place, it is doubtful whether a single purchasing office is even now a sensible objective. In this respect the committee seems almost as ready as the government to think of computers as nine-day wonders. Purchasing is at present coordinated by a strange amalgam of committees, with Her Majesty's Stationery Office looking on. Is there any substitute, in what are supposed to be days of professional management in government, for an arrangement under which the government's agency of financial administration — the Civil Service Department — arbitrates between users ? Is it sensible to recommend a system of national preference without providing some guidance about the degree of preference which is justifiable ? And if this unwelcome doctrine is to be stomached at all, might it not be wise to think of it in a European context ? In the long run, a sensible pattern of high technology in Europe will emerge only when European governments are not ashamed to buy each other's products, which argues for European and not national protection.

The thinnest part of the Select Committee's report is that dealing with research and development. To be sure, the committee is entirely right to complain that the British Government's spending on research and development, most probably less than £6 million a year, is far too small. On the other hand, it is brash to suggest that government expenditure on research and development should promptly be raised to £50 million a year, roughly ten times the present scale of expenditure. One obvious difficulty is that there is very little experience to suggest how such expenditure should be organized. The time has gone when military contracts could help with the development of civil computers. In Britain, the attempt in the past few years to use the National Physical Laboratory as a focus for creative research and development has not been a roaring success. There might be something to be said for an identifiable planning body, representing government and industry, to work out a specific policy for research in computing and related fields, but the suggestion that there should be a Computer Research and Development Board consisting of five independent people with a licence to spend £50 million a year is a mixture of wishful thinking and irresponsibility.

If there are funds on such a scale available, it would almost certainly be better to spend them on setting up an organization to provide the software without which computer purchasers cannot use the machines they buy. To the extent that software is an essential in selling hardware, such a development would also suit the manufacturers. The immediate need, in other words, is for a suitably strong commercial organization. In the long run, the best hope may be to persuade government departments to put out to tender more of their software development. That may be the best of all the Select Committee's proposals.

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100 Years Ago

The Origin of Insects

In an article by Dr. Beale, in your number for Nov. 23, on "One of the Greatest Difficulties of Darwinism," a most extraordinary misconception is stated to be a difficulty. That the pupa state is a modification of the ordinary process of skin-shedding in the Insecta is proved by so many facts, that one cannot understand for a moment how it can possibly be denied, much less how its denial can be made use of as an argument against the doctrine of evolution. Sir John Lubbock pointed out long ago that, in the development of the Insecta, every grade of modification exists between those insects which are gradually developed, each successive ecdysis producing only the slightest possible modifications, and those which undergo a change so complete that it may be likened to the process of metagenesis, as it has been called, which takes place in the Echinodermata.

It is an utter mistake to suppose that any insect is redeveloped during the pupa state. The most perfect instance of metamorphosis is that of the flies (some Diptera). In these the materials out of which the perfect insect is developed are supplied by the breaking up of the muscular system and fat bodies of the larva ; but the cellular structures known as the Imaginal discs of Weismann are formed in the egg, and persist all through the life of the larva. These, it is true, only form a skin or case in which the fly is developed ; but they are really nothing more than a larva skin, formed on the inside of the larva skin in the egg, and detached from it by the subsequent modifications of the larva.

From Nature, **5**, 101, *December 7*, 1871

What Future for High Energy Electron Physics ?

ONE of the proposals for discussion at today's (December 3) meeting of the European Committee on Future Accelerators (ECFA) in Geneva is that an electron accelerator should be built to cater for the needs of European physicists in the late 1970s and 1980s. The most likely outcome is that a working party will be set up to examine the feasibility of the project.

The proposal will be put by Professor A. Ashmore, director of Daresbury Nuclear Physics Laboratory, who knows as well as anybody that the Science Research Council, having agreed to support the 300 GeV accelerator now being built at Cern, will not also be able to finance the 20 GeV synchrotron that had been planned for Daresbury and for which the present 5.0 GeV electron accelerator (NINA) would have been an injector. Professor Ashmore is also only being realistic in now pressing for a European rather than a British machine, as the cost of independence in such a large project is becoming increasingly prohibitive for any country.

Professor Ashmore's proposal is likely to have a mixed reception although the affiliated ECFA countries are certain to agree, on scientific grounds alone, that there is an obvious need for a high energy electron accelerator. But feet will drag because the proposal comes so soon after the allocation of money for the 300 GeV accelerator. The possibility of alienating public opinion is the fear among the diplomats of high energy physics. But a feasibility study would entail little financial drain on any national budget, and its terms of reference are unlikely to be more specific than the consideration of the type of accelerator needed in Europe ten years from now.

The future of the Daresbury laboratory and the Rutherford High Energy Laboratory at Chilton seems to be assured for the next five years, although it is not clear what will happen afterwards. In 1972–73 the Rutherford laboratory will cost the SRC £7.2 million and the Daresbury laboratory £3.2 million—essentially the same as they will cost in 1976–77. Budgets are reviewed annually, however, and there is always a chance that support might be withdrawn before then. In the current year, the SRC will contribute £1.2 million towards the construction of the 300 GeV machine and £7.0 million for experiments with the present facilities at Cern. Five years from now, £5.8 million is earmarked for the 300 GeV machine and £3.2 million for the other facilities. Inflation apart, the total British contribution to CERN will be kept constant at £9.0 million a year after 1972–73.

Manpower threatens to be as restricting as money. Unless there is an increase in the number of high energy physicists within a year or so, there will be too few British scientists to make effective use of both international facilities and Cern accelerators. There are at present 350 high energy physicists in Britain of whom 80 are electron physicists at Daresbury. About half of the total are graduate students and according to Professor J. C. Gunn, University of Glasgow, chairman of the nuclear physics board of the SRC, there are no plans to increase this number.

It is not possible at present to say whether either the Rutherford or the Daresbury laboratories—or even both—will have to be closed to allow full British participation in the 300 GeV project, which will need 1,000 scientists when it is in full operation. A decision will have to be made before 1976, however, and electron physicists will be more directly affected than the present users of NIMROD or the 28 GeV proton synchrotron at Cern. This is why the people directly concerned are anxious that the course of electron high energy physics for the next decade be marked out as soon as possible. The only machine in Europe comparable with NINA is the 6 GeV electron synchrotron at the Deutsches Elektronen-Synchrotron laboratory in Hamburg (DESY), but that laboratory is at present being improved by the addition of two storage rings that will raise the maximum energy available to 9 GeV.

High energy physicists are pressing for a decision on the future of electron physics against their better judgment. They realize that unless a plan for the future is agreed on soon, there is a danger of an unbridgeable gap between the end of NINA's useful little life—or much sooner if it is decided that NINA be sacrificed on the altar of the 300 GeV machine—and the time when a new facility could become operational. Even if a decision were taken now to go ahead with a design study on a European electron accelerator, there would be a hiatus after useful physics on NINA is brought to an end. Professor Ashmore is concerned that the hiatus does not develop into an unbridgeable chasm.

What are the alternatives facing the electron physicists if NINA, for one reason or other, is axed? One promising suggestion involves an electron beam obtained from a proton accelerator. In this way, for example, 100 GeV electrons can be obtained from the reaction

$$\pi^\circ \rightarrow 2\gamma \rightarrow e^+ + e^-$$

if the π° particles are produced by 300 GeV protons. These electrons can be

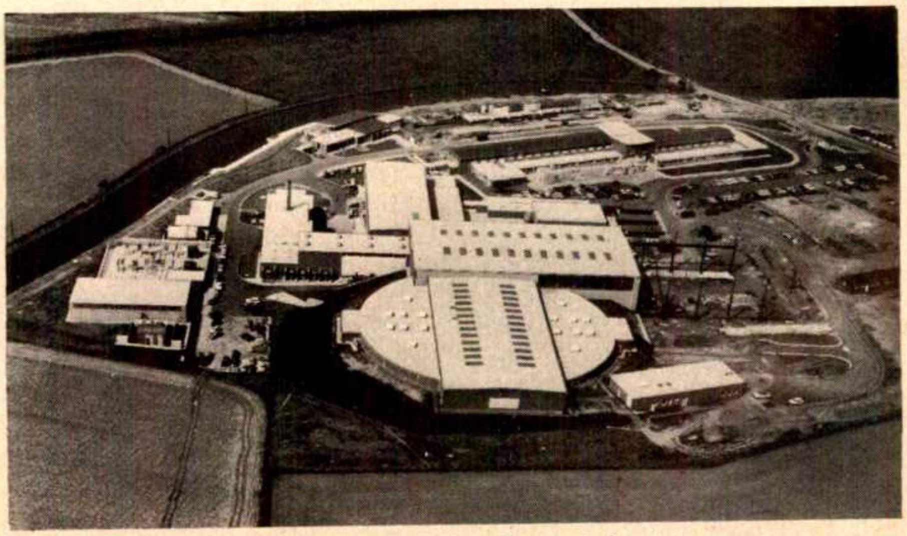

Fig. 1 Daresbury Nuclear Physics Laboratory.

used to study the deep inelastic continuum with an energy that is not at present a practical proposition with a conventional electron accelerator. The drawbacks are that the beam intensity would be low and that its optical quality would leave much to be desired, but the high energy is an attraction.

It is also possible that British electron physicists could collaborate after the end of NINA's useful life with either the scientists at DESY or at the Stanford Linear Accelerator Center. Such associations, however, could only be a temporary arrangement to bridge a gap before an accelerator that British physicists could use by right became operational.

A suggestion at present circulating among high energy physicists does not involve the building of a new facility. It is proposed that a small electron accelerator—perhaps of a few GeV—should be used to inject electrons into the intersecting storage rings (ISR) at Cern. The advocates of this scheme already have a machine lined up—the 2.5 GeV accelerator nearing the end of its useful life at the University of Bonn. Such a combination of the ISR and a small electron machine could produce electrons of 15 GeV in the centre of mass system, but the intensity of the beam would be low, and large aperture detectors can compensate only to a certain extent. Even so, a detailed study of this proposal needs to be carried out.

Nothing less than a new accelerator that will produce a beam of several hundred microamps of electrons will satisfy most high energy electron physicists, even if in the long run they may have to make do with something less. To win allegiance in the 1980s, an electron accelerator will have to produce at least 40 GeV electrons. How might that be done? A report published last December by M. C. Crowley-Milling of the Daresbury laboratory (*High Energy Electron Accelerators: Cost Comparisons,* DNPL, TM/78) compares the cost of constructing different types of electron accelerators. The summary of his calculations, shown in Fig. 2, reveals several interesting facets, not the least of which is the competitive cost of superconducting linear accelerators. His calculations show that a synchrotron is the cheapest way to produce an electron energy up to 35 or 40 GeV. For 40 GeV and above, there is no clear choice and estimates for synchrotrons, superconducting linear accelerators and hybrid combinations of synchrotrons and linear accelerators become similar—all being about £30 million (compared with the £100 million for the 300 GeV facility at Cern).

The optimistic estimate for the superconducting linac (*c*) is based on a voltage gradient of 10 MV per foot, whereas the other estimate (*b*) is based on a gradient of 4.3 MV per foot—the aim at the High Energy Physics Laboratory (HEPL) at Stanford University.

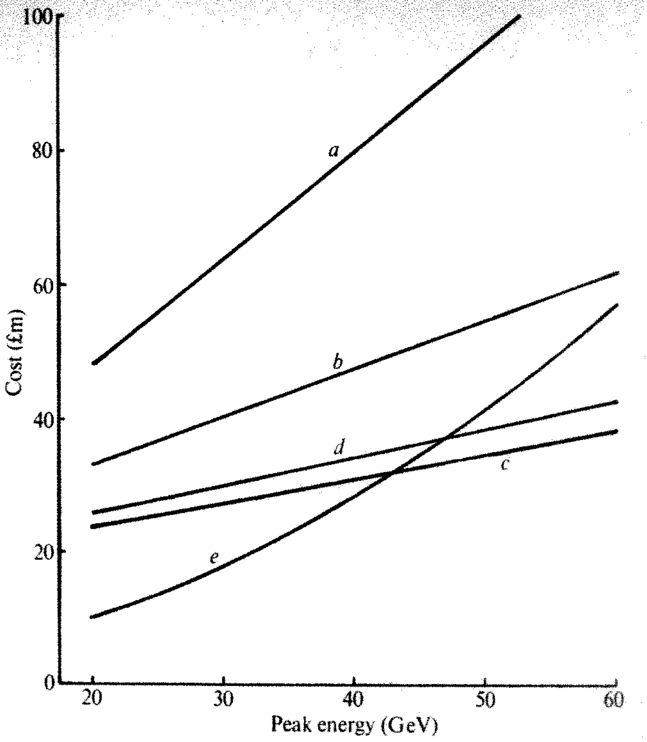

Fig. 2 Cost of electron accelerators after M. C. Crowley-Milling. *a*, Stanford Linear Accelerator; *b*, superconducting linear accelerator; *c*, superconducting linac (optimistic); *d*, mesotron; *e*, synchrotron.

The accuracy of these estimates, made before any practical experience had been available from superconducting machines, is being questioned because of the setbacks now being experienced at HEPL. Professor H. Alan Schwettman confirmed last week that there are problems with the voltage gradient in the accelerator. The sections of the machine already installed have been run at gradients of 1 MV per foot—a long way short of the planned 4 MV per foot—and there have been difficulties in raising the voltage because of magnetically weak points on the cavities and excessive field emission.

There is cheerful news, however, in that 10–20 microamps have already been run through the test sections—not far short of the 100 microamps the accelerator is designed to carry. Superconducting accelerators are not out of the woods yet, however, and time—and possibly an infusion of money—will be needed before the Stanford machine achieves its design rating. At present it looks as if the SLAC estimates of 10 MV per foot are exceedingly optimistic and that superconducting linear accelerators will continue to be more expensive than conventional synchrotrons for a long time.

Perhaps the most interesting and practical accelerator to achieve electron energies greater than 40 GeV is a synchrotron–linear accelerator combination that has been called a mesotron. In such a machine, two linear accelerators are connected by a series of bending magnets to return the beam through the machine several times. The advantage of a mesotron over the synchrotron is that it is much easier and cheaper to increase the energy at a later date.

Another possibility would be to build a synchrotron to give 30 GeV to 40GeV, but to increase this energy at a later date by putting in radio frequency power. A more economic way of doing this would be to inject the extracted beam into a linear accelerator to give a final energy of 50 GeV at a much lower cost than needed to obtain this energy by a linear accelerator or a synchrotron alone.

The situation will be much clearer if and when a decision is needed on a European accelerator. In particular the success or failure of the Stanford HEPL accelerator project will have been assured and the cost will then be less of an estimate. At this stage it is certainly opportune to ask whether another accelerator is in the best interests of the high energy community in Britain. Without doubt, involvement in a further European accelerator project will ensure that British national laboratories will no longer house large accelerators. There will not be enough people to man them, to say the least of things. An electron accelerator at 40 GeV or more can be justified on scientific grounds alone, but the 300 GeV project has shown that scientific merit is not a deciding factor when governments are asked to finance such expensive projects.

OLD WORLD

UNESCO

Work for Pruning Hooks

THE discussion of Unesco's Man and the Biosphere programme in Paris last month resulted in the thirty-one research projects that the conference met to discuss being cut to thirteen. The thirty-one projects were the result of a Unesco general conference as long ago as November 1966 which authorized the preparation of a research programme on the rational use and conservation of the resources of the biosphere. The thirteen projects which have finally emerged will now be considered by the twenty-five national committees of the participating nations which will decide which projects they will support and to what extent.

Before the meeting, doubts had been expressed about the effective need of the programme, particularly in Britain and the USA, but the reaction of the British delegates to the conference—although this may not prove to be the reaction of the national committees—is that the meeting was effective and constructive. Dr M. E. D. Poore, Director of the Nature Conservancy, declared himself "quite well satisfied with progress made" as the programme that emerged is much more precisely defined and practicable. The thirteen projects that have emerged range from studies of ecosystems in rivers, islands, mountains and forests to studies on the effects of engineering work, energy use and population movements on man and his environment.

During the conference, the emphasis changed from considering man set against the biosphere to considering man as an integral part of it who simply has a greater power than other organisms to alter it for better or worse. The relationship between the natural sciences and the social sciences received greater emphasis in the final projects—one is concerned with how man's perception of environmental quality varies from place to place.

One reason the conference was so successful is that the delegates, although representing governments, were largely scientists rather than administrators, and thus the final programme is felt to be more practicable and profitable than might otherwise have been the case.

No cost estimates are available for the projects as yet, and it is doubtful if they will involve large amounts of expenditure that would not otherwise have occurred. Where the programme is likely to have greatest effect is in the exchange of findings between countries and in the prevention of duplication. Additional finance may well be provided by developed countries working in participation with developing countries to initiate studies on, for example, desert and forest ecosystems. This was the basic philosophy on which the International Biological Programme—which is not government sponsored—ran, and of which the Man and the Biosphere programme is to a certain extent the continuation.

Once the national committees have decided the extent of their involvement a detailed programme will be produced for confirmation by another conference in March 1973, although work on the projects may well start before then.

INFLUENZA

Beating the Bug

BRITISH health authorities expect outbreaks of influenza this winter to be worse than last year's comparatively light outbreaks. Large numbers of cases have already been reported on the continent, particularly in Spain and eastern Europe, and *Pravda* reported last week that the Soviet Union is expecting outbreaks soon. In Britain, people at special risk have been advised to arrange vaccination quickly. These include people with chronic lung complaints, heart conditions and glandular disorders. The influenza strain is the same as last year's—the A2 Hongkong virus which first appeared in 1968 and which affected eight million Britons two years ago. Vaccines at present available give protection against all current strains of influenza for about seven months. An attack of influenza, however, gives immunity to that particular strain for between six months and two years, which partly accounts for the light outbreak last year. Antibody levels in the population last year meant that about 70 per cent of the population had some sort of protection but this has now fallen to about 40 per cent.

There are three serotypes of influenza (A, B and C), each with subtypes. Antibody levels against type C are naturally high and at worst it only produces mild colds. The A and B strains are the ones that produce the epidemics. Both these strains mutate slowly and continuously so that new vaccines have to be introduced every few years to allow for the change, but A strains also mutate abruptly every seven to ten years—as in 1968 with A2 Hongkong and in 1957 with A2 Asian. It is these sudden mutations that tend to produce the really bad epidemics as it takes three to four months to produce commercial quantities of a new vaccine. From studies on pigs which have caught A2 Hongkong from man it is thought that the A strain influenzas may be animal viruses which have crossed the species barrier into man.

The vaccines used in Britain are the inactive type. Formalin or betapropiolactone is used to inactivate the virus, leaving the antigens still present on the surface to build up the blood's antibodies. The vaccines do not, however, guarantee immunity. The Department of Health and Social Security says they are only 40 to 60 per cent effective but the manufacturers claim an efficiency of about 70 per cent. The discrepancy is probably due to the conditions under which the vaccine is tested and to the fact that a number of conditions produce symptoms similar to those of influenza and these cases are unjustly put down to vaccine failure.

Perhaps the best hope in the control of influenza lies in live virus vaccines which are already in use with mixed success in the Soviet Union. Work on live vaccines began in Britain in 1957 at the Common Cold Research Unit in Salisbury. The principal problem is that a virus in a vaccine must be sufficiently attenuated not to give the recipient influenza and yet active enough to be effective. Live vaccines under tests are producing immunity levels of almost 100 per cent, although they produce lower antibody levels than inactive vaccines. Commercial application of live vaccine is still some years away, however, as careful tests are needed to ensure that the attenuated virus does not revert to its wild state during use. If and when live vaccines become available they will be much cheaper than the inactive vaccines as about 10,000 doses can be produced from one egg as compared with one dose of inactive vaccine.

Satellite Delays

THE launching of the ESRO satellite, HEOS-A2, scheduled for December 10 has been postponed until January 1972 at the earliest. The reason is that NASA is still investigating the cause of the recent failure of the ITOS-B launch and no Delta rocket launchings will take place until the end of the investigation. NASA has confirmed that in spite of the delay it will still attempt to launch the next scheduled ESRO satellite at the end of February, as originally planned.

The launching of the UK-4 satellite originally planned for November 29 has been put back once again. The launch, which has now been twice postponed because of a fault in a monitor in the University of Iowa experiment, is now planned to take place from the Vandenberg test base in California on December 9.

NEW WORLD

HIGHER EDUCATION

Funding in Limbo

by our Washington Correspondent

CAUGHT in the usual pre-Christmas backlog of legislation, the Senate has decided to put off until January at the earliest further consideration of bills designed to increase funding for institutions and students in higher education. The chief reason for the delay is that early in November the House of Representatives passed a bill that is so different from legislation passed by the Senate in August that there will be a lengthy fight in the Senate even before a conference committe is given the formidable task of sorting out differences between the bills. Consequently, the whole issue has been sent back to the Senate Committee on Labor and Public Welfare for its consideration.

Apart from the sharply differing philosophies that are embodied in the versions of the bill passed by the House and the Senate, senators are concerned about the fact that measures for desegregating schools, and in particular amendments opposing the busing of children from one school to another to achieve a racial mix, were tacked onto the bill passed by the House. The Senate passed its own desegregation bill earlier this year, and will probably combine the two pieces of legislation to have a consistent policy to take to a conference committee. In addition, Senators who are opposed to busing have promised to try to put the anti-busing amendments passed by the House into the Senate bill.

While these skirmishes over desegregation are going on in Congress, college administrators will be anxiously looking on to see how Congress will deal with their interests. The chief point to be resolved is whether the conference committee will finally decide to distribute federal support for higher education in the form of grants to institutions or of grants to students. The House version called for general grants to institutions, distributed largely on the basis of the total number of students at each university or college, while the Senate bill would establish the right of each qualified student to receive $1,400 minus the amount that his family would be expected to contribute.

Although colleges will not be badly affected by the delay in agreeing on the legislation, since appropriations for 1972 have already been agreed on, a long delay next year would present some difficulties for planning budgets for the 1972–73 academic session. Those involved in the legislation are predicting that it will take several weeks to sort out the differences.

Horrendous Problems

IN his last annual report as President of Massachusetts Institute of Technology, Dr Howard W. Johnson has issued a stern warning of the financial problems that lie ahead for higher education. Dr Johnson's bitterness at past funding policies in higher education is evidenced by these extracts from his annual report for 1970–71:

"I have spoken in each of my annual reports on the problems of financing MIT. We are a special place, and we fare a bit better than many others. But the financial problems ahead for higher education are horrendous. Increasing tuition must continue in the face of rising costs, but I, for one, fear that such a continuation will bear most heavily on the large middle group of our students that fall in the financial range between the very needy and the very affluent. I fear that a steadily rising collegiate budget could eventually prevent many of them from attending MIT. There is a very real need here that has not received adequate attention by anyone in higher education.

"We must maximize our efforts at raising private resources. The satisfaction of investment in private education is still there despite the occasional uneasiness for some that accompanies the support of youth. But quality institutions need federal support in addition, and new forms of that support must be devised if the long-term interests of our society are to be protected."

Dr Johnson's warnings could well be directed at the Administration which should, if a conference committee can sort out the differences in bills passed by the House and the Senate, soon be considering a Congressional proposal to give federal grants to institutions of higher education.

Short Notes

Enzyme Detergents

A COMMITTEE appointed by the National Research Council—the operating arm of the National Academy of Sciences—has come to the conclusion that "the average enzyme detergent laundry product in normal use by consumers has not produced more primary irritation of the skin than have similar products that contain no enzymes". Commissioned by the Food and Drug Administration, the study bases its conclusion on the fact that only six cases in which there is unequivocal evidence of allergic reactions associated with use of enzyme detergents came to the committee's attention during the course of its extensive investigations.

The committee found, however, that some workers in plants that manufacture detergent products who have been exposed to relatively high concentrations of dust containing enzyme materials have suffered respiratory tract and skin injuries. The symptoms range from irritation and coughing to breathlessness, sometimes lasting for several hours. But the committee suggests that the average consumer would be exposed to such low doses of the enzyme materials that he or she would not be affected. The study has found immediate acceptance in at least one quarter —the day after the study was published, Procter and Gamble issued a press release saying that "we hope these findings by the nation's most respected scientific body will serve as the ultimate reassurance to housewives and will finally put to rest the unfounded charges which have been made against the consumer safety of enzymes". The report was one of the first of the NRC publications to bear the new label to the effect that responsibility for all aspects of the report rests with the study committee.

Technology and Foreign Policy

THE National Science Foundation has awarded the Brookings Institution a grant of $125,000 to study "the impact of technological change on American foreign policy and prospects for world order". The study, which will be directed by two members of the Brookings foreign policy staff, will be concerned with a broad range of questions such as new ways for exploiting seabed resources, telecommunications, and weather prediction and modification. Environmental pollution and the depletion of scarce resources are two other areas which will come under study. The chief object of the exercise will be to determine for each area studied what new forms of international organization and regulation will be required.

New Man at OST

EDWARD E. DAVID jun, the President's Science Adviser, has a new special assistant for national security matters. The first incumbent of the newly created post will be John B. Walsh, a former member of the Secretary of the Air Force's research and development staff, and a specialist in missile systems. Walsh will work directly with David and with Dr Henry Kissinger, Assistant to the President for National Security Affairs.

Where To Go After Mars

by our Washington Correspondent

FLUSHED with the success of Mariner-9's encounter with Mars, space scientists are again beginning to talk with some conviction about the merits of taking a closer look at Jupiter and the outermost planets of the solar system. Soon after Mariner began sending photographs of the Martian dust storm, for example, Dr Robert S. Kraemer, director of NASA's planetary programmes, took the opportunity to call a press conference to remind the public that Pioneer 10 is scheduled for launch to Jupiter early next year, to reach the planet in December 1974, and that it would be followed a year later by Pioneer 11.

These flights, Dr Kraemer reminded his audience, are essential to chart part of the course for the much more ambitious "Grand Tour" of the planets—Jupiter, Saturn, Uranus, Neptune and Pluto—to be launched between 1976 and 1979 (Jupiter, Saturn and Pluto first and then Jupiter, Uranus and Neptune). One much publicized feature of the Grand Tour is that the special alignment of the outer planets that enables one spacecraft to visit three planets in succession comes round once every 179 years.

The recent flurry of interest drummed up in the Grand Tour possibility is being widely interpreted as an indication that NASA officials are trying to sell the idea to the Office of Management and Budget in time to get an increase in funding for development of the TOPS (thermoelectric outer planet spacecraft) in the 1973 budget request. Negotiations between NASA and OMB are now in a critical stage, and if the 1976 and 1977 launches are to go ahead, there will have to be a strong financial commitment to the programme in the near future. NASA officials should be helped in their negotiations by a study published last week by the National Academy of Sciences* which concludes that exploration of the outer solar system should be "one of the major objectives of space science in this decade".

But there is no complete agreement within the scientific community—or even among planetary scientists themselves—on the merits of pressing ahead with the Grand Tour. The broad argument is whether the Grand Tour would soak up so much of NASA's scientific budget that the whole programme would get out of balance, with smaller but worthy projects being squeezed out. Some planetary scientists also argue that a programme based on an intensive study of Jupiter would pay a better scientific dividend than would a quick look at the outer planets.

In a great many respects, the academy report takes account of all these points of view, for while tub thumping for the Grand Tour, it also points out that the project should not be undertaken at the expense of intensive study of Jupiter nor at the expense of other scientific projects in NASA's overall programme. But perhaps the chief value of the report is that it presents NASA with a range of options from the full-scale Grand Tour to a watered down version, depending on the level of available funds. A report on priorities in space research, published by the academy

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Outer Planets Exploration 1972–1985, Space Science Board, 2101 Constitution Avenue, Washington DC 20418.

Hard Way to Jupiter

by our Washington Correspondent

IN February or March next year, Pioneer 10 will be launched on a journey that should take it past the orbit of Mars, through the asteroid belt, to Jupiter and then on to the edges of the solar system. The chief object of the exercise is to take a close look at Jupiter, but just how close the look should be has developed into something of a controversy. Present plans are to take the spacecraft in to about three Jupiter radii, but the working group on outer planetary research of the Space Science Board has suggested that it should be brought as close to the surface as quarantine specifications allow—about 1.3 Jupiter radii. Even at that distance the intensity of the particle flux trapped in the planet's magnetic field may be so great that the craft's instruments could be put out of action.

Why should planetary scientists suggest that a spacecraft costing nearly $100 million should be destroyed by taking it so close to Jupiter? The argument hinges on the importance of assessing the intensity of Jupiter's radiation, to see what sort of a hazard it poses to later exploration of the planet or even to the Grand Tour. Those who argue for taking Pioneer 10 close to the surface point out that even if the instruments are destroyed, most of the scientific work would already have been done, and the choice is really between studying Jupiter's radiation belts or the interplanetary medium beyond Jupiter. Since Pioneer is not designed for a long lifetime, it is difficult to predict how much of the interplanetary medium would be surveyed before its signals become too weak to pick up.

The question was, however, brought up during a meeting of planetary scientists at NASA's Ames Research Center on November 11. According to Dr Charles F. Hall, project manager for the Pioneer programme, the consensus of that meeting was that the distance of closest approach should be kept at about three Jupiter radii on the basis that although the absolute level of the energy and flux of protons in the radiation belts are poorly known, the rate of change of energy with distance from the planet is much better known. In other words, the information relayed back from Pioneer 10 can be extrapolated to determine absolute radiation levels closer to the planet.

Radiation damage is, however, only one of the hazards the Pioneer 10 and other craft venturing much beyond the orbit of Mars must encounter. Before the spacecraft arrives at Jupiter, it must spend about six months crossing the asteroid belt, where it stands about a ten per cent chance of severe or even final damage. During its passage through this belt, two instruments will be set the task of scanning asteroids and measuring the mass and energy of tiny particles impinging on the spacecraft.

Once through the asteroid belt, Pioneer 10 will travel on to Jupiter, reaching the planet in December 1974. Instruments will sample the proton and electron flux, and measure the energy output from the planet with an infrared radiometer, which should also map the temperature distribution and provide some answers about Jupiter's enigmatic red spot, and a magnetometer will measure the planet's magnetic field. Beyond Jupiter, the spacecraft will send back data on the interplanetary medium and cosmic rays, until its signals become too weak to monitor when it reaches about 2,000 million miles past Jupiter.

earlier this year, said in effect that the Grand Tour should not be undertaken unless NASA's budget for scientific research were to increase by 50 per cent —a criterion that placed the project lower on the shopping list than most planetary scientists would like.

Prepared by a study group of the Space Science Board (a committee of the National Academy of Sciences that provides advice and commentary to NASA on space science), under the chairmanship of Dr Francis S. Johnson, of the University of Texas, the report addresses itself specifically to the question of whether or not the chief thrust of exploration of the outer planets should be to undertake an intensive study of Jupiter or to flit round all the outer planets, taking a first look at each. The philosophical argument boils down to the practical question of how best to apply a limited amount of money. The Grand Tourers argue the value of a quick look at hitherto uncharted planets and their satellites, especially in preparation for fuller studies. The special alignment of the planets in the 1970s and 1980s also provides a unique opportunity to get to the outer planets quickly and relatively cheaply, and such a mission would also keep plenty of steam in the planetary exploration programme.

Those who argue for a more intensive study of Jupiter (and to a lesser extent Saturn) suggest that there are already theories about the planet that are crying out for direct observation, and that Jupiter has many features—such as a magnetic field and a magnetosphere—which merit intensive study. And there is also the prospect for taking a close look at the satellites of Jupiter and Saturn.

Linked with the recommendation for more intensive study of Jupiter and Saturn as opposed to the Grand Tour is the suggestion that, even though the opportunity for taking in several planets and their satellites in one mission will not recur before the middle of the 22nd century, nuclear electric powered spacecraft, which would considerably shorten flight times to the outer planets, could be developed in the 1980s. The chance of studying the outer planets will therefore not be completely foreclosed by not taking up the Grand Tour option.

The latest academy report attempts to reconcile these points of view by sailing a middle course, concluding that "a programme combining TOPS Grand Tour with the more intensive study of Jupiter and Saturn with flybys, probes, and orbiters is fully justified". Specifically, the study group recommends that if NASA's budget for planetary exploration were to increase to about $400 million a year, four TOPS Grand Tour missions should be flown between 1976 and 1980, two of which would carry entry probes. Alongside this programme, however, the study group suggests that Pioneer-type spacecraft should be developed for carrying probes and orbiters to Jupiter and Saturn, with about two launches a year.

An important peg in the study group's recommendations is that the exploration of Jupiter and Saturn with the less sophisticated Pioneer-type spacecraft should not be subject to the budgetary axe to accommodate the Grand Tour, and accordingly the report recommends a series of cuts in the Grand Tour programme as the budgetary horizons for planetary research contract. Essentially what the report suggests is that the number of missions should be reduced to three or to two, in preference to reducing the payload, but that as a last resort the payload should be cut down to 130 lb. If NASA were to embark on even this scaled down version of the Grand Tour, however, it would require a quite substantial increase in the funds devoted to planetary research, and the study group suggests that the floor of the outer planetary research programme should be a study of Jupiter with Pioneer-level spacecraft, including turbopause probes and perhaps deep entry probes to Jupiter and Saturn, and orbiters to Jupiter. At all budgetary levels, the report suggests that the seven-segment Titan rocket should be developed, and that nuclear electric and solar electric propulsion should receive some funding to provide the capability to reach the outermost planets in the 1980s.

These recommendations are subtly different from a set of options listed in a major report of the Space Science Board published in March this year (see *Nature*, **230**, 142; 1971). That report set out to provide NASA with a list of priorities in its space science budget, given different levels of funding, and it suggested that the Grand Tour should not be considered unless NASA's space science budget were to increase by 50 per cent—in effect, the report recommended the full Grand Tour or nothing, and given the present economic climate, Grand Tour enthusiasts knew they would get nothing. The latest report, however, provides a more flexible approach including a watered down but still scientifically exciting economy class Grand Tour—the scaled down version could be accommodated without unbalancing the space science programme if NASA's space science budget were to grow to 125 per cent of its present value, the study group suggests.

Key feature of the Grand Tour project is the TOPS spacecraft—a thermoelectric spacecraft that must have a lifetime of at least ten years, a computer that can test and repair itself, and a capability for carrying scientific payloads of at least 130 lb. Full development costs are expected to be about $440 million, and conversion to probe carrier and orbiter will add about another $20 million and $130 million respectively to the bill. Because the Grand Tour option is tied to a specific date, the most crucial question now emerging is how long a full-scale start on the TOPS spacecraft can be delayed before the option on the Grand Tour is missed.

NASA's budget for the present financial year contains $20 million for development of TOPS, but the project has not yet had Congressional approval. If the 1976–77 launch window is not to be missed, there will clearly have to be a larger financial commitment to TOPS development in the budget now being put together in the White House, with the understanding that the budget for 1974 would include another sharp increase. Whether the OMB, let alone Congress, is prepared to swallow such an increase is doubtful at present, but to judge by the recent proselytizing of NASA officials, the agency is clearly staking a considerable amount on outer planetary exploration.

What effect is the academy's study likely to have on the prospects for the Grand Tour? Even the chief participants in the study are unwilling to answer that question, but it seems likely that one effect will be that NASA will not let the Grand Tour go ahead to the exclusion of other projects—both the priorities report and the latest report were insistent on that point. Dr Herbert Friedman, who was chairman of the executive committee which produced the priorities report, said last week, for example, that "Dr Fletcher is very objective about all of these questions and insists that his people pay high regard to external advice from sources such as the National Academy", and Dr Michael B. McElroy of Harvard University said that he would be "very disappointed if we did not take advantage of what is essentially a unique opportunity"—but quickly added that he would be even more disappointed if in going for the Grand Tour option the space science programme became unbalanced.

Similar sentiments were also expressed by Dr George Wetherill, of the University of California at Los Angeles. Pointing out that to miss the Grand Tour option would take a greater deal of steam out of planetary exploration, and that the option of developing a nuclear electric spacecraft for outer planetary exploration would probably delay the exploration of planets beyond Saturn until the 1990s, Dr Wetherill said that the Grand Tour offers a unique opportunity for space research. "One area that has not been given adequate discussion," Dr Wetherill suggested, "is the question of priorities in the whole NASA programme, for example, between the Grand Tour and the shuttle."

NEWS AND VIEWS

Neuronal Uptake Processes

IT is now well established that the transmission of information in the nervous system generally involves chemical rather than electrical relays. At synaptic junctions the transmission of impulses is effected by the release of minute amounts of chemical transmitter substances which diffuse across the narrow gap separating the presynaptic and postsynaptic cells to trigger either excitation or inhibition of activity in the postsynaptic element. Acetylcholine and noradrenaline have long been known as the transmitters involved in the peripheral nervous system, but in the central nervous system it seems likely that these substances play only minor parts in the chemical transmission of impulses at synapses. The amino-acids such as gamma-aminobutyric acid (GABA), glycine, glutamate and aspartate probably represent the more important transmitter substances in the brain and spinal cord.

The use of an amino-acid, such as glycine or glutamate, as a neurotransmitter poses certain problems because in addition to this postulated specialized function these substances are also present in all living cells and serve important functions in metabolism, and as precursors for protein synthesis. The neurones that use such amino-acids as transmitters must therefore be faced with certain delicate logistical problems in the handling of the amino-acids for several different functions within the same cell.

The ubiquitous occurrence of amino-acids such as glycine or glutamate in all the cellular elements of the central nervous system also poses very difficult technical problems to the biochemist who is interested in studying the small compartment of amino-acid likely to be associated with neurotransmitter functions. On page 297 of this issue of *Nature*, however, Logan and Snyder suggest one way in which such studies may be made possible. These workers have studied *in vitro* the uptake of radioactive amino-acids by nerve terminal particles ("synaptosomes") in homogenates of rat brain and spinal cord. Analysis of the kinetics of amino-acid transport for seven common amino-acids revealed that in spinal cord homogenates three amino-acids—glycine, glutamic acid and aspartic acid—showed two kinetically distinct components in their uptake. One component was of relatively low affinity (apparent Km approximately 1–4 mM) whereas a second component could be distinguished as having a much higher affinity (Km approximately 0.02 mM).

In the spinal cord there is evidence that all three amino-acids may serve a transmitter role. The other four amino-acids which Logan and Snyder tested—alanine, arginine, leucine and serine—showed only a single component in their uptake in both spinal cord and cerebral cortex homogenates. This component was of the "low affinity" type. In the cerebral cortex homogenates, glycine exhibited only the low affinity component in its uptake; other evidence suggests that this amino-acid functions as a transmitter only in the spinal cord and lower brain stem. There is thus an apparent correlation between a functional role of amino-acids as neurotransmitters and the existence of high affinity uptake processes. Similar high affinity uptake processes have been described for other neurotransmitters, such as noradrenaline, serotonin, dopamine and GABA (for review see Iversen, *Brit. J. Pharmac.*, **41**, 571 ; 1971). The special high affinity uptake process for glycine in spinal cord was also described in slices of this tissue by Neal and Pickles (*Nature*, **222**, 679 ; 1969) and Neal (*J. Physiol.*, **215**, 103 ; 1971).

In the case of the uptake of noradrenaline, the uptake process is known to be associated with adrenergic nerve terminals and seems to have an important physiological function in terminating the released transmitter by a process of "recapture". There is also evidence that the uptakes of dopamine and serotonin are specifically associated with neurones which use these substances as neurotransmitters. Recent autoradiographic studies on the location of radioactive GABA after its uptake by brain slices and homogenates have indicated that this uptake may also be associated with a specific population of neurones, possibly corresponding to those which use this amino-acid transmitter (Hökfelt, *Brain Res.*, **22**, 391 ; 1970; and Bloom and Iverson, *Nature*, **229**, 628; 1971).

There is thus some reason for optimism in hoping that the special uptake processes associated with the transmitter functions of amino-acids in the central nervous system may prove invaluable studies of these systems. It is possible that uptake processes represent the mechanisms by which transmitter actions at synapses are generally terminated, in which case the metabolic inactivation of acetylcholine at cholinergic synapses will prove to be the exception rather than the rule. Whatever the physiological significance of such processes is, there seems little doubt that they will prove to be extremely valuable for investigations of the transmitter functions of amino-acids in the central nervous system.

The existence of high affinity uptake processes for common amino-acids such as glycine and glutamate suggests that it may be possible to achieve a selective incorporation of the labelled forms of these amino-acids into the transmitter pools, provided appropriate concentrations of exogenous amino-acid are used. At sub-saturating concentrations uptake will occur far more rapidly by the high affinity components than by the low affinity systems. Logan and Snyder's article which reveals the existence of high affinity uptake systems for glutamate, aspartate and glycine in nerve terminals is thus potentially of considerable significance to workers interested in neurochemical studies of transmitter systems in the central nervous system.

Phase Transitions go Bang

THE notion that earthquakes and some other geological processes, volcanoes for example, may be triggered off by the explosive release of energy is a little like an explanation in search of something to explain. On page 293 of this issue of *Nature*, Professor A. F. M. Barton and his colleagues return to a theme which seems first to have been started by Professor A. R. Ubbelohde more than twenty years ago. Although the specific energy release in the solid–solid phase transitions likely to occur in the Earth's crust is small, when cubic kilometres of material may be involved, it is clear that very large amounts of energy may be made available. Moreover, in several laboratory systems—Barton *et al.* give a list of some of these, the polymorphic transitions in antimony and of austenite to martensite, for example—it does seem that phase transitions can be rapid, sometimes explosively so.

Most contributors to this discussion have assumed that in the crust or mantle of the Earth, a phase transition would spread through a body of rock consisting of a metastable phase as would a shock wave. But where would the metastable phases have come from? The suggestion now is that the way in which the material of the oceanic crust is carried beneath continental margins in the process of continental drifting provides a continually replenished source of metastable rocks, the energy released from which may provide the driving force for some of the earthquakes which occur with foci at considerable depths beneath the continental margin. The explanation is ingenious and attractive. The greatest difficulty is that of reconciling the pattern of energy release recorded by seismometers, which usually implies that shearing mechanisms are responsible for the deep focus earthquakes, with the notion that energy might be released in large volumes of material by explosive phase transitions. In other words, there seems to be a source of energy in the mantle but no geophysical evidence to suggest why it should be invoked.

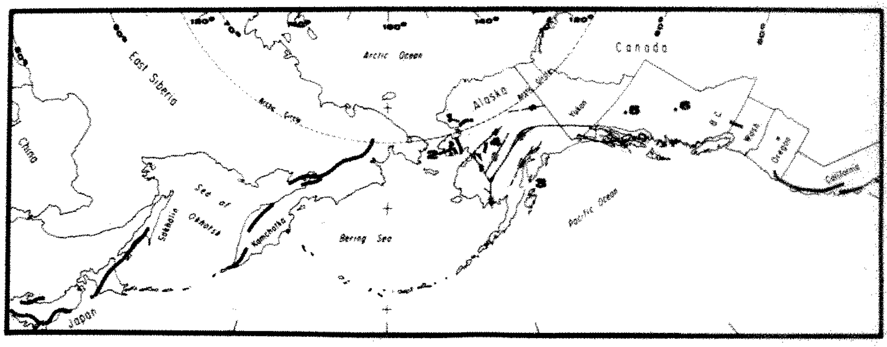
Is it necessary to let such an intriguing possibility go begging? For some time now, it has been clear that more needs to be done to understand the consequences of phase transition in geological processes. Earlier this year, Dr D. R. Waldbaum (*Nature*, **232**, 545 ; 1971) argued that temperature changes accompanying the phase transitions in the mantle might be of great importance. His particular point was that the Joule–Thomson coefficients for many of the materials of which the mantle is made are likely to be negative at the pressures which occur in the Earth's crust, which implies that adiabatic decompression would bring about an increase of temperature and the release of heat even when no phase transitions are involved.

Although there is some dispute about the precise significance of Waldbaum's argument and about the likelihood that adiabatic processes do actually occur in the mantle of the Earth, this is yet another means by which the appearance of large amounts of energy deep in the interior of the Earth may be explained. This is why it seems quite clear that there is a need for more detailed and more accurate studies of the thermodynamic properties of rocks at high pressures as well as of the kinetics of phase transition in bulk materials.

For the time being, these are the directions in which speculation about explosive phase transformations in geology might be given a firmer basis. In short, even if there is not yet a crying need for the use of these explanations, they may at least serve as stimulants of valuable research.

Tectonic Implications of Blueschists

A FEW years ago Blake *et al.* (*Tectonophys.*, **8**, 242 ; 1969) noted that blueschist facies rocks seem to occur in narrow tectonic belts in association with ultramafic rocks; and this fact led them to suggest that the metamorphism which produced them may have occurred during underthrusting in a zone of anomalously high water pressure. If so, such metamorphism may be expected to occur most frequently along continental margins where oceanic crust is underthrusting and being subsumed, or even where such processes once took place but have now ceased. Such an expectation is especially attractive because blueschist facies metamorphic belts are also known to be associated often with ophiolites—an association thought to be characteristic of oceanic crust.



Map (polar projection) of western North America, north-east Siberia, Kamchatka and Japan (Hokkaido and Honshu), showing the regional distribution and location of blueschist facies metamorphic belts.

In next Monday's *Nature Physical Science* these speculations are placed into some sort of perspective by Forbes *et al.*, who report new discoveries of blueschists in Alaska and use these discoveries to show that blueschist terranes form a well-defined belt around the northern Pacific margin. The accompanying map shows the blueschist facies metamorphic belts current recognized, including the Alaska terranes (1–4) and those recently discovered in Canada (5–6) by Monger (*Geol. Surv. Canada* Paper 68–48, p. 12 ; 1969) and Paterson (unpublished hitherto).

This is not the first time that blueschists have been discovered in Alaska ; but what Forbes and his colleagues have done is to show that the scale of the Alaskan blueschist terranes is far greater than previously suspected. In fact, there now seems to be one large belt of blueschist metamorphism stretching from the Seward Peninsula (site 2) to the Baird Mountains (site 1). The Kaiyuh Mountain site (4), on the other hand, seems to form an isolated terrane although later discovery may link it to the Seldovia terrane at site 3.

Forbes and his colleagues say that their report is a preliminary statement of the new discoveries; and thus they do not discuss tectonic implications in any detail. What does seem to be clear, however, from the distribution of blueschist metamorphism around the Pacific is that it is the result of global, rather than purely local, tectonic processes.

ENZYMES

Push-button Control

from our Molecular Biology Correspondent

ENZYMOLOGY is clearly getting harder every day. Time was when one enzyme was considered to do one job, and the only legitimate objective of the enzymologist was to find out how. An increasing number of enzymes are now coming to light which can be switched on, off, or even into other modes, in response to triggering ligands. A very advanced model is that described by Meister and his colleagues (Trotta *et al.*, *Proc. US Nat. Acad. Sci.*, **68**, 2599; 1971). This is a carbamyl phosphate synthetase which, like other members of the family of glutamine amidotransferases, utilizes the amide group of glutamine for various synthetic functions. It is a characteristic of this group of enzymes that they are also able to make do with ammonia, though this is turned over with lower efficiency.

The *Escherichia coli* carbamyl phosphate synthetase puts together its end-product from glutamine, bicarbonate and ATP and intermediate steps in this process can also be isolated. The enzyme is controlled by several positive and negative feedback ligands, which are formed at the ends of the synthetic pathways in which it is involved. Trotta *et al.* have now demonstrated that the molecule consists of two subunits, estimated by detergent-gel electrophoresis to have molecular weights of 42,000 and 130,000. These chains could be dissociated, separated, and then recombined to give a substantially native product.

Examination of the activities of the separated subunits showed the following: neither chain alone was capable of the synthesis of carbamyl phosphate from glutamine, nor of the partial reaction of glutamylhydroxamate hydrolysis in the presence of ATP and bicarbonate. The large subunit, on the other hand, was active in carbamyl phosphate synthesis from ammonia rather than glutamine, and also in another partial reaction—the hydrolysis of ATP in the presence of bicarbonate. Both chains individually retained the glutaminase function. The various activators and inhibitors still exert their control over the activity of the large subunit, which therefore evidently contains the relevant binding sites. The function of the small subunit is surmised to be the binding of glutamine to a site at which it can be attacked by a nucleophile, which by an affinity label experiment with a glutamine analogue is inferred to be a thiol group. Trotta *et al.* suggest from a comparison of related enzymes in other species that the small subunit may represent an evolutionary refinement, in which ammonia was supplanted as the main nitrogen source by glutamine. A test of this hypothesis would be a structural comparison of glutamine-binding chains from the related enzymes of other species.

A system with great biochemical appeal just now are the cyclic AMP-dependent protein kinases, which have been identified in a number of tissues. These seem always to consist of two subunits, one catalytic and one regulatory, and the word now is that the cyclic AMP operates by binding to the latter. In Krebs's laboratory a direct demonstration of this scheme in the rabbit skeletal muscle enzyme has now been achieved (Brostrom *et al.*, *ibid.*, 2444). Two kinases, differing somewhat in molecular weight, are present in the tissue. Each consists of a regulatory and a catalytic subunit, and it is only the former which differ in size. Mole for mole the two proteins are identical in AMP binding capacity. When cyclic AMP is added to the enzyme, the subunits dissociate, and can be separated chromatographically, the ligand being then found only on the regulatory chain. Short of denaturation, the bound cyclic AMP could not be removed from the protein, except by addition of an excess of the catalytic subunit, when it was forthwith displaced.

It seems then that there the system functions by a disproportionation mechanism: cyclic AMP will bind to the regulatory subunit, and thereby displace it from its partner, or the catalytic subunit may bind to the regulatory chain, with displacement of the cyclic AMP. In practical terms the liganded regulatory subunit when added to the intact kinase increases the cyclic AMP concentration required for a given level of kinase activity. If some agency (insulin being an interesting candidate) were to cause a diminution in cyclic AMP concentration, the equilibrium between the kinase subunits would shift in favour of association, and the activity would become more sensitive to the cyclic AMP that remains. Brostrom *et al.* suggest that the complex with the regulatory subunit may be the form in which the cyclic AMP is kept in readiness in the cell. The next step will be to measure the concentrations of the two subunits actually present.

The protein kinases in liver have been studied by Chen and Walsh (*Biochemistry*, **10**, 3614; 1971). They are three in number, two, of apparently identical molecular weight, being cyclic-AMP-controlled, and a smaller one, which is not. The preponderant heavy component is heterogeneous, in that catalytic subunit can be resolved into two components. The smaller kinase is evidently an isolated catalytic chain, but is not identical with the other catalytic subunits. On the other hand, it will combine functionally with isolated regulatory subunits. Chen and Walsh note that there are many synthetic functions in the liver which might be expected to be regulated by cyclic AMP, and might therefore call for the presence of different specialized protein kinases.

Peptide Map of Chimpanzee Haemoglobin

THE haemoglobins of higher primates are very like those of man. In the chimpanzee it is thought that all the three major polypeptide chains (α, β and γ chains, the last of which is the foetal analogue of the β chain) have identical sequences to the corresponding human molecules. Moreover, the γ-chain exists in two forms, one with glycine, the other with alanine at position 136, in monkeys, apes and man. Again the chimpanzee possesses the minor adult component, A_2, which has the structure α_2, δ_2, just as in humans, and it is the δ-chains which are the subject of a sequence study by De Jong, reported in next Wednesday's issue of *Nature New Biology*.

The tryptic peptide map of chimpanzee δ-chains is identical with that of human δ-chains, except for one peptide. The substitution turns out to be val-126 for the met-126 found in man. It is highly probable that there are no other differences between the sequences. The replacement corresponds to a point mutation (GUG→AUG) which would have occurred after evolutionary divergence, valine occupying the corresponding position in the molecule in all known primate α, β and γ-chains, and also in the δ-chains of some New World monkeys. (Old World monkeys seem to have no haemoglobin A_2.)

Calculations have shown that the rate of evolutionary mutation in mammalian haemoglobins is one substitution for 100 residues every 10^7 years. With 725 residues in the normal haemoglobin chains (α, β, two types of γ and the δ) altogether, the statistically predicted extent of mutation would be one residue between all of them every 1.4 million years. The divergence time for hominids is variously reckoned to be between 4 and 14 million years ago, and De Jong argues that the absence of any replacements whatever since divergence is good evidence in favour of the shorter time.

PALAEOANTHROPOLOGY

Descent of Man

from a Correspondent

THE hundredth anniversary of the publication of Darwin's *The Descent of Man* set the theme for the symposium for the study of human biology held on November 19 at the Hospital for Sick Children, London. Professor J. S. Weiner (London School of Hygiene and Tropical Medicine), in a retrospective book review of Darwin's second major work, showed Darwin's remarkable foresight in predicting many features of human evolution which have subsequently been verified. Darwin's suggestion that man arose from a tropical African ape has found firm support not only in the fossil record but also in the more esoteric fields of molecular and biochemical investigations.

Dr D. Ferembach (University of Paris) was unable to attend, but his contribution, which suggested that in man and certain animals bone growth and bone morphology can be affected by dietary and caloric deficiencies during crucial growth periods, was read for him. Dr Ferembach questioned whether these effects may not have influenced morphological differences in living human groups. Dr C. Oxnard (University of Chicago), in a largely theoretical paper, discussed new analytical tools for the investigation of skeletal form. Medial axis transformation and Fourier optics were among the techniques he described as "optical dissection". Dr H. Preuschoft (University of Tübingen), in a biomechanical investigation of certain East African fossil primates, suggested that "*Proconsul*", an important Miocene form, was strictly quadrupedal with no locomotor specializations for arboreal life.

Dr G. Olivier (University of Paris), in a restatement of the concepts of nineteenth century French anthropology, discussed the relationship between "hominization" and brain development as reflected in cranial capacity. Dr J. Musgrave (University of Bristol), using the results of a multivariate analysis of the hand of Neanderthal man and certain Upper Palaeolithic *Homo sapiens*, suggested that the two groups showed important anatomical differences in hand structure (see *Nature*, **233**, 538; 1971). He further suggested that the Neanderthal hand, with its wide hand and short, broad phalanges, may have been cold adapted.

Dr M. H. Day (Middlesex Hospital Medical School) presented a discussion of Middle Pleistocene femora including the recently published *Homo erectus* femur from Olduvai Gorge (*Nature*, **232**, 383; 1971). The great similarity between Olduvai Hominid 28 and the Peking femora has thrown further doubt on the provenance and relationships of the "*Pithecanthropus erectus* I" femur from Java. This specimen, which is stratigraphically associated with the *Homo erectus* skull cap from Trinil, has long been thought to show essentially modern morphology. Dr Day further suggested that the "*Pithecanthropus erectus* VI" femur, probably from Kedung Brubus, is not hominid at all and is possibly carnivore. Miss T. Molleson (British Museum (Natural History)) discussed a variety of analytical and relative dating techniques used on the Javan femora in an attempt to define more clearly their provenance and date. The tests, using fluorine, uranium and nitrogen levels, have all been inconclusive as far as dating is concerned.

Undoubtedly the most important occasion of the day was the presentation by Mme and Dr Henri de Lumley (Marseilles University) of the new Arago material. In an almost unprecedented gesture, the participants in the symposium were able to examine the original specimens. The Arago Cave is situated in the south-eastern French Pyrenees near the town of Tautavel. In a Tayacian level, dated through its geology and fauna to the earliest Riss (about 200,000 BP), a partial skull with a complete face and two mandibles have been found. The parietals and occiput of the skull are missing and an apparent stone tool remains fixed by matrix within the skull cavity; the face shows only slight damage and distortion. This skull is of great importance because only two other faces of Middle Pleistocene times are known; one, Steinheim, is badly distorted and today, thirty-eight years after its discovery, it remains unprepared and inadequately described, and the second, "*Pithecanthropus* VIII" from Java, has only recently been reported and is so far incompletely prepared and described (S. Sartono, *Proc. Ned. Akad. Wet.*, Ser. B, No. 2; 1971). At present it is obviously impossible to discuss the affinities of the Arago material. Its attribution, by the de Lumleys, to a "pre-Neanderthal" group is attractive at this stage in that the term reflects what is quite possibly its transitional nature.

Subsolidus Reduction of Lunar Spinels

A FEATURE of lunar rocks that sets them apart from their terrestrial equivalents is that they crystallized under extremely low partial pressures of oxygen. This has resulted in the virtual absence of ferric iron and in the widespread occurrence of troilite (FeS) and metallic iron. A less obvious consequence now seems to be the reduction suffered by certain spinels after crystallization. Compositional variations in lunar spinels were recently discussed by S. E. Haggerty in *Nature Physical Science* (**233**, 156; 1971) and in a communication in next Monday's issue he enlarges on this aspect.

Apart from a small isolated group of chromian pleonasts, all lunar spinels so far described belong to a series extending, with decreasing titanium content, from ulvospinel (Fe_2TiO_4) towards chromite ($FeCr_2O_4$); in addition, there is some substitution of Mg for Fe and of Al for Cr. Re-examination of Apollo 12 material and a study of samples from Apollo 14 and 15 show the widespread occurrence of spinel-ilmenite-iron intergrowths. The ilmenite ($FeTiO_3$) forms lamellae along octahedral planes in the spinel and is accompanied by blebs of free iron.

Haggerty interprets the intergrowths not as true ex-solution effects, which they resemble, but as subsolidus reduction. Not all spinels in the series exhibit these intergrowths but only those, in any one sample, towards the ulvospinel end—as revealed by probe analysis. Examples are found further towards the chromite end in samples from Apollo 14 than in those from Apollo 15 or 12, and further still in fragments of crystalline rocks from breccias than in unfragmented rocks. The subsolidus reduction of the spinel meant that it became increasingly enriched in the chromite end-member as Fe and Ti were removed to form more and more metallic iron and ilmenite.

Consideration of available thermodynamic data allows the oxygen fugacity to be plotted against temperature for the dissociation of the pure end-members ulvospinel, ilmenite, hercynite ($FeAl_2O_4$) and chromite, and shows that of these minerals chromite is the most stable, ulvospinel the least. Ulvospinel can dissociate either partially to ilmenite and iron, or completely to rutile and iron. The fact that only partial dissociation is observed would seem to set close limits on the fugacity/temperature conditions. In one sample examined, the decomposition of a fayalitic olivine (Fe_2SiO_4) to symplectic metallic iron and cristobalite provides confirmation of a very low oxygen fugacity, as the theoretical dissociation curve lies between those for the partial and complete dissociation of ulvospinel.

Haggerty holds that the decomposition observed indicates lower oxygen fugacities than those prevailing during crystallization. The reduction may have occurred during initial deuteric cooling, but the fact that the breccias are more intensely reduced than the crystalline rocks suggests that it may be related to contact with meteoritic iron vaporized during impact events.

CONTRACTILE PROTEINS

Muscular Platelets

from our Cell Biology Correspondent

Now that an actin-like protein, which may well prove to be completely identical to muscle actin, has been found in considerable amounts in nerve cells (*Nature New Biology*, **234**, 115; 1971) where it may be responsible for the motility of the growing tips of axons, it comes as no surprise to read in the current issue of the *Proceedings of the US National Academy of Sciences* (**68**, 2703; 1971) that Adelstein, Pollard, and Kuehl have isolated a myosin-like as well as an actin-like protein from human blood platelets.

Platelets play a crucial part in wound healing; they cause the retraction of clots and clearly such a contractile function must depend on some sort of molecular contractile apparatus. It is several years now since so-called thrombosthenin—a complex mixture of contractile proteins—was isolated from platelets but successive attempts to isolate actin or myosin-like proteins from this material have resulted in failure. Adelstein and his colleagues have, however, now succeeded in this by dissolving thrombosthenin in a buffer containing Mg^{2+}, ATP and dithiothreitol and fractionating it by ammonium sulphate precipitation followed by chromatography and polyacrylamide gel electrophoresis.

By these procedures they have isolated proteins which can be classified as myosin-like by several criteria. The myosin-like protein from platelets, for instance, binds both muscle and platelet actin; it has an Mg^{2+} dependent ATPase activity and in the electron microscope it can be seen to have the characteristic structure of myosin with a rod and a head portion, the head portion binding actin. Furthermore, the major polypeptide chain of platelet myosin has a molecular weight of about 200,000 daltons, the same as that of rabbit skeletal muscle myosin. As Adelstein *et al.* comment, the predominance of head and rod portions of myosin molecules in their preparations suggests that platelet myosin is probably subject to proteolytic cleavage either exclusively during its isolation or *in vivo* before isolation. The suggestion that thrombin may be responsible for the cleavage of thrombosthenin proteins in platelets has, of course, been made repeatedly in the past.

Apart from intact myosin and myosin head and rod pieces, the fourth chief protein which Adelstein *et al.* have isolated from thrombosthenin assembles into filaments 6 nm wide which form "arrowhead" complexes with platelet and skeletal myosin. This protein has the same molecular weight as skeletal muscle actin, 46,000 daltons, and it contains one 3-methylhistidine residue per molecule. For these reasons Adelstein and his colleagues believe it is an actin.

Clearly, fingerprint analyses of these two platelet contractile proteins and, ultimately, analyses of their amino-acid sequences will have to be made in order to establish their complete identity or otherwise with their skeletal muscle counterparts. But from the evidence currently available it is reasonable to conclude that the molecular basis of contraction in platelets is in all essentials similar to that of skeletal muscle.

MATERIAL SCIENCE

Metal Matrix Composites

from a Correspondent

THE objective of a symposium on November 15 at the Liverpool Polytechnic on the subject of metal matrix composite materials was to bring together research workers and potential consumers for an exchange of current views on the usefulness of these composite systems and possible future developments. It was clear that although experimental work (such as that described by Dr B. Harris of the University of Sussex) is still being carried out on metals reinforced with strong metal wires, present interest is largely in systems in which carbon fibres or refractory whiskers or fibres are the reinforcing agents. The obvious reason for this is the potential saving in weight to be gained from using these light fibres instead of the denser metallic reinforcements.

The dominant theme of the symposium was undoubtedly the problem of the high temperature instability of carbon fibres and whiskers in contact with matrix metals such as nickel and aluminium. Experiments with carbon fibres have so far seemed to concentrate on the use of nickel or aluminium as the matrix metal. Dr S. J. Harris (University of Nottingham) explained that on the basis of cost, density and general properties, the aluminium/carbon fibre system is probably the most promising for study, and he described the methods used at Nottingham and Rolls Royce for producing good composites. He discussed the properties of these materials, in comparison with such competitors as boron fibre-reinforced aluminium and whisker-reinforced aluminium, but was forced to conclude that experimental strengths are often lower than theoretically obtainable values, usually because of fibre damage during manufacture.

Work on carbon fibres in nickel described by Dr W. Bonfield (Queen Mary College, London) and Mr P. Ormiston (University of Southampton) left listeners with the impression that the lack of high temperature compatibility in this system, which leads to fibre degradation especially in the presence of oxygen, probably precludes its commercial use unless some means could be found of introducing an efficient diffusion barrier between fibre and matrix. There was considerable discussion of the

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Specificity of mRNA Degradation

How messenger RNAs are degraded in bacteria and how the degradation process is regulated remain vexed questions. There is, of course, no shortage of hypotheses and there are one or two enzymatic activities which are likely candidates for the job of cutting messenger RNAs to pieces, but the biochemistry of the process remains to be fully elucidated and its elucidation is clearly not going to be any easy matter. As Marrs and Yanofsky report in next Wednesday's *Nature New Biology*, different messengers in the same *Escherichia coli* cell are degraded at different rates and this observation leads them to suggest that the rate of degradation of any messenger may be partly determined by its particular structure.

Marrs and Yanofsky have measured the half-lives of phage T7 mRNAs and tryptophan operon messengers in *E. coli* cells infected with an amber mutant of T7, am193. This phage, because of the amber mutation it carries, does not make its own T7 RNA polymerase and as a result the phage late genes are not expressed. All RNA synthesis in the cells infected with am193 is carried out by the *E. coli* DNA dependent RNA synthetase and so it is sensitive to inhibition by rifampicin.

Using this experimental system Marrs and Yanofsky have compared the synthesis and survival of the early T7 messengers and the *E. coli* tryptophan operon messengers in the same cell. In short, they find that whereas the T7 messenger RNAs have half-lives of some 6 to 20 minutes, the trypE messenger RNA has a half-life of a mere 80 seconds in the infected cells as it does in normal uninfected *E. coli*.

Marrs and Yanofsky's observation clearly indicates that the enzymatic machinery responsible for degrading messenger RNAs attacks different classes of messengers at different rates; in other words, the degradation machinery must be able to distinguish one messenger from another and any hypothesis seeking to account for the turnover of messengers must be able plausibly to account for this fact.

mechanisms of degradation, and the role of oxygen in this process but, perhaps surprisingly, nothing at all was said of current experimental work on the development of interface barrier coatings. In metal matrix/metal fibre composites the problem of intermetallic formation at the interface, with possible deleterious effects, especially on fatigue properties, is also a serious difficulty. Some elegant experiments on wetting of ceramics by molten metals and alloys were described by Dr J. A. Champion (National Physical Laboratory). These experiments yield the kind of information that designers of composites may need when considering particular combinations of materials for specific purposes.

The only contribution which dealt with the industrial viewpoint—that of the design engineer—was given by Dr M. A. McGuire (GKN Group Technological Centre). He described two case studies in the development of metal matrix composites and outlined a model approach to designing with composites that might be considered as a substitute for conventional materials in simple engineering applications. The general conclusion—not an encouraging one for most of the participants—was that as far as the engineering industry is concerned, metal composites can scarcely hope to compete with metals—and particularly with steels—on economic grounds.

The symposium ended with some interesting ideas put forward by Mr R. W. Jones (Liverpool Polytechnic), who suggested that glass-ceramic fibres might be used as reinforcements for metals. The particular advantages of glass-ceramics over glass are that higher elastic moduli can be obtained; modulus and expansion coefficient can, within limits, be tailored to suit a particular matrix; and they are less susceptible to weakening through surface damage. Difficulties of making good strong fibres are yet to be overcome, however.

MATERIALS SCIENCE

Coating Processes

from a Correspondent

THE topic of coatings was considered at this year's autumn meeting of the Materials Science Club held in Great Malvern on November 11 and 12. In an introductory talk Dr J. E. Castle (University of Surrey) described the principal features of surfaces as boundaries between solids, and liquids or gases, and he outlined some recent work on Auger and low energy electron diffraction spectra of surfaces. This work suggests that impurities of surfaces are often different from those in the bulk material and that significantly different crystal structures can exist in the near surface regions.

Chemically and electrochemically applied coatings on metals were the subject of talks by Dr C. J. L. Booker (City of London Polytechnic) and Mr R. Walker (University of Surrey). Conversion coatings are essentially methods of thickening or modifying the natural oxide coating of metals, by chemical or anodic treatments, to improve the degree of protection. These are widely applicable to steel, aluminium, magnesium, titanium and their alloys. The simplest treatment is known as the simple dip process which has been developed to produce coatings suitable for painting and as lubricating and corrosion resistant finishes in their own right.

Anodizing is a more sophisticated form of treatment which allows considerable control over the thickness and structure of the film produced, even to the extent of allowing colour decorative effects to be produced by optical interference in thin transparent films of titanium alloys. Electrodeposited coatings are perhaps the most widely applied metal coatings. The Pourbaix diagram provides the useful indication of optimum plating conditions. Acidic baths are usually preferred, on economic grounds, but in some instances complex electrolytes are required to ensure satisfactory deposits. The important properties in plated coatings are adhesion, porosity, internal stress and brightness, which may be controlled by attention to the preparation of the substrate, and by control of the *p*H, temperature and current density of the plating solution. In particular, complex additives often have a profound effect on the quality of the deposit. Mr Walker outlined the beneficial effects of benzotriazole on the internal stress and brightness of copper and nickel deposits plated from acidic baths.

Dr R. L. Apps (Cranfield Institute of Technology) described his work on the adhesion of sprayed aluminium coatings on steel and concluded that the grit blasting stage of substrate preparation was all important. Impurities derived from grit debris seem to reduce adhesion, and plasma sprayed coatings were better than those deposited by oxy-acetylene flames. Dr R. F. Smart (Associated Engineering Developments Ltd) also discussed plasma sprayed deposits. The great advantage of this technique is that almost any material can be sprayed and with suitable pre-

Octanoic Acid and Photosynthesis Inhibition

THERE is a remarkable difference between the *in vivo* and *in vitro* absorption spectra of bacteriochlorophyll *a* (BChl). In organic solvent this pigment has a single far-red absorption band at 770 nm whereas *in vivo* BChl can have several peaks in the 800 to 900 nm region. The spectral shift almost certainly results from the hydrophobic protein environment in which the BChl is sited within the bacterial membranes.

In next Wednesday's issue of *Nature New Biology*, Steffen and Calvin discuss experiments which demonstrate that concentrations of fatty acids which are known to inhibit photosynthesis do so by interacting with the pigment-protein complex responsible for channelling light energy to the reaction centres.

Steffen and Calvin have used chromatophores isolated from the blue-green mutant of *Rhodopseudomonas spheroides* strain R26. This photosynthetic bacterium has a BChl absorption peak at 590 nm and a single far-red peak at 860 nm (B590–860). Treatment of the chromatophore preparations with *n*-octanoic acid at concentrations below 10^{-2} M and at low *p*H causes the far-red absorption band to shift to 770 nm (B590–770). This shift is not caused by an acid or *p*H effect because HCl does not bring about a similar spectral change. With higher concentrations of octanoic acid both the 590 and 860 nm bands are shifted towards the blue with new peaks at 530 and 760 nm (B530–760). The B590–770 resembles the BChl spectrum *in vitro* and B530–760 corresponds to the spectrum of bacteriopheophytin (BChl which has lost its central Mg ion).

There was no evidence that *n*-octanoic acid detaches the pigment from its protein carrier, and, moreover, the absorption shifts were reversed on the removal of octanoic acid. Steffen and Calvin argue that their spectral observations result from the protein-pigment complex unfolding in the presence of fatty acids so as to expose the BChl molecules to the solvent. Measurement of fluorescence depolarization and of light-dark difference spectra showed that this unfolding decreases the efficiency of energy transfer between the light harvesting BChl molecules resulting in an inhibition of reaction centre (P890) oxidation.

NMR studies indicate that octanoic acid molecules interact weakly with the chromatophore membrane and that the polar carboxyl group is not involved in the binding. Steffen and Calvin in fact have additional evidence for hydrophobic interaction because the neutral ester methyloctanoate can act in the same way as octanoic acid.

cautions pore free deposits, up to several hundred microns in thickness, may be produced. Principal applications are chemical and wear resistant coatings, reclamation, and thick film electronic circuitry.

Three other high temperature coating processes discussed were vacuum coating, diffusion coatings and pyrolytic coatings. Dr L. Holland (Edwards High Vacuum Ltd) described the principal vacuum coating techniques with particular reference to R. F. Sputtering which has proved to be a most versatile method. He outlined the range of materials which can be processed and the quality of the deposits which can be produced. Pyrolytic coatings of refractory metals may be deposited by chemical or thermal breakdown of their volatile halides, and carbon and silicon carbide from hydrocarbon and silane gases respectively. Dr E. H. Voice (OECD Dragon Project) described the Dragon nuclear fuel pellet as an example of the use of the technique. The pellet consists of a sphere of uranium oxide or carbide coated with two layers of pyrocarbon interspersed with one of silicon carbide; the total diameter is about 1 mm. The coatings are applied by a fluidized bed technique. Dr N. A. Lockington (Chrome Alloying Co. Ltd) devoted most of his talk to the chromizing process, in which a chromium rich layer is diffused into the surface of the ferrous material or nickel alloy. The most advantageous method is to use a pack process; the components are packed in an inert medium (alumina) containing ferrochrome and a halide. On heating, the halide acts as a transport medium to move chromium from the ferrochrome to the component. Several other processes operating on the same principle are feasible but apart from siliconizing, which is used to produce disilicide coatings on superalloys, they are not important commercially.

Non-metallic coatings discussed included paints and plastic coatings on metals. Dr L. H. O'Neill (Paint and Varnish Manufacturers Research Association) described several new developments in paint finishes, including thermosetting acrylic finishes which should prove to be more durable than thermoplastic acrylic lacquers now widely used as car finishes. Domestic paints containing both urethane and silicones which combined fast drying and non-drip qualities with good durability are also being developed. Dr O'Neill also discussed an intriguing development which aims to replace a conventional white pigment by a suspension of bubbles to produce an opaque finish, but these finishes have so far proved to be too soft for commercial use. Plastic coatings may be applied to metals by dipping the preheated metal part into either a fluidized bed of polymer powder or into a liquid plastisol. The former process is applicable to polyethylene, nylon and unplasticized PVC, whereas the latter is applicable only to plasticized PVC compounds. Dr G. E. Barrett (Plastic Coatings Ltd) described the precautions necessary to obtain good adhesion and satisfactory coatings. He also discussed the requirements of the polymer to render it suitable for the process. These requirements are very severe and virtually limit the fluidized bed process to low density polyethylene and nylons 11 and 12, which have the necessary wide melting range and easy flow properties without degradation.

Dr A. Rantell (Polytechnic of the South Bank) spoke on metal plated coatings on plastics. These coatings are produced by a conventional electroplating technique preceded by etching and chemical deposition stages. The essential pretreatment is the deposition of a minute quantity of palladium on to the plastics surface. This acts as a catalyst for an electroless nickel plating process which in turn provides a substrate for the conventional electroplate. Adhesion is controlled by an initial etching process. Experience has shown the most suitable substrate material to be ABS, the rubber phase of which may be etched out to provide an excellent mechanical key for the plate. More recently, techniques have been developed for plating polypropylene and nylon with satisfactory results, the basic problem being to provide a suitable surface at the initial etching stage.

Dr D. White (Houldsworth School of Applied Sciences, University of Leeds) described coatings formed by dipping metal articles into suspensions of clay minerals. Thin coatings of montmorillonite have been found to give excellent protection against oxidation on steels, and titanium alloys. This is sufficient to allow them to be heat treated at temperatures up to 750° C without other forms of protection. The exact mechanism of protection is not clear but it is known that very thin films (about 1 μm) are effective. These coatings are very cheap and easy to apply.

At the meeting the A. A. Griffith silver medal for 1971 was presented to Professor J. White (University of Sheffield) and the Materials Science Club Prize was presented to Mr S. Turner (ICI Ltd, Plastics Division).

Evolutionary Behaviour of Quasars

In attempting to fit the observational data of quasars at radio and optical wavelengths to a reasonable cosmological model, it is necessary to assume some form of evolutionary behaviour of the sources. Different workers have, however, disagreed about the precise nature of this evolution. For instance, Schmidt has claimed that only the population density of quasars is time dependent whereas the luminosities are constant, and Rowan-Robinson maintains that either density or luminosity evolution is present, but in both optical and radio properties. On the other hand, Arakelian has claimed not only that density evolution is absent, but that the optical and radio properties evolve differently.

The different conclusions of these workers are a consequence of their different ways of analysing the data (chiefly from the 3C catalogue). Rowan-Robinson has used the luminosity-volume test in which the numbers of sources in a given range of radio or optical luminosity are counted for different redshifts. Schmidt's procedure was to calculate the average value of a ratio of volumes, one corresponding to the redshift of a particular source, the other corresponding to the redshift at which such a source would disappear at the survey limit. A uniform distribution will give a value 0.5. The new feature introduced by Arakelian was to treat the optical and radio data separately. Using Schmidt's data and method as well as the 4C catalogue he found only radio (but not optical) luminosity evolution.

Arakelian's results have been subject to some doubt, and a reconciliation of the conflicting conclusions is presented in an article in next Monday's *Nature Physical Science* by L. M. Golden of the University of California. Golden points out that Arakelian's work suffers from a selection effect. Thus for a representative radio (optical) sample, those of low optical (radio) luminosity will be observed only at small redshifts. Arakelian has apparently also used a non-representative sample, and so Golden has repeated Arakelian's analysis, correcting for these effects. For this Golden essentially uses only the bright sources, and assumes an Einstein–de Sitter cosmology (although the conclusion is insensitive to the value of the deceleration parameter). The result is that the radio/optical luminosity ratio is independent of redshift for a least squares fit, indicating similar evolution at both wavelengths.

Using this result, Golden also points out that Schmidt's analysis in fact permits both luminosity and density evolution. In this way the results of all three procedures can be reconciled.

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Acoustics of Insect Song

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This article describes the state of knowledge about insect sound production and hearing with special reference to *Drosophila* and some larger insects.

MOST animals communicate acoustically using a transducer which causes vibrations in the medium around them. These vibrations can be received at a distance by a vibration sensitive receptor on another animal. By producing a patterned train of vibrations, the animal producing the sound can provide a species specific or a context specific signal which may be important in the sexual or social behaviour of the animal.

Other aspects of such songs may be of considerable importance to the animal because of the limited bandwidth available, for example one species tends to hear the songs of another. Also, in the case of a small animal, the range of the songs may be small and so it may be advantageous to produce a directional sound output and one that is adapted to the acoustic receptor. But the complexity of vertebrate songs and of the sound producing and receiving mechanisms means that it is difficult to study the acoustics rigorously.

Many insects, however, produce songs comprising nearly pure tones and do so by a mechanism which can be excited artificially and described in physical terms. For these reasons, the study of insect acoustics is informative. But from the biologists' standpoint it has another interest because insects are small animals and communicate with sounds whose wavelength may be many times the length of their bodies; in these conditions the acoustic power can be minute and the song may have a degree of intimacy unknown in vertebrates.

Sound Waves

Many of the problems encountered in insect song have been examined either theoretically[1] or in the context of acoustical engineering[2]. Sound is propagated as a series of waves of compression and rarefaction; there is little absorption of energy and so power is radiated over a considerable distance. If acoustic power radiates from a point into a free space, a spherical wave is propagated and the acoustic power at a distance decreases as the square of the distance from the source. Sound intensity, the power per unit area, measured normal to the source is the product of the pressure and the particle velocity in the wave[2].

In acoustics it is often convenient to consider the specific resistance of the medium, expressed in kg m^{-2} s^{-1}, which is the product of the density of the medium, ρ, and the velocity of sound, c. In a manner analogous to electrical power, acoustic power can also be considered in terms of the sound pressure or of the particle velocity. The power per unit area is given by

$$I = pu = u^2\rho c = \frac{p^2}{\rho c}\ \text{W m}^{-2} \tag{1}$$

where p is the pressure in N m^{-2} and u is the particle velocity in m s^{-1}. Sound power is often measured in decibels (dB) where 0 dB$=10^{-12}$ W m^{-2}. This is equivalent to a pressure of 2×10^{-5} N m^{-2} or a particle velocity in a plane wave of 0.5×10^{-7} m s^{-1}.

As with electrical power, this relationship only holds if the pressure and velocity terms are in phase. In a plane wave, or at a large distance from a point source, pressure and particle velocity are in phase, but as the distance from the source decreases to about the wavelength of the sound, the divergence of the waves must be considered. In this condition, the spherical wave, the particle velocity and the pressure are no longer in phase[2] and the phase angle can be obtained from

$$\text{Tangent phase angle} = \frac{\lambda}{2\pi r} \tag{2}$$

where λ is the wavelength and r is the distance from the source. Thus the phase angle between the pressure and the particle velocity increases towards 90° as the source is approached; this has important consequences when small sources are considered.

The acoustic power from a point source in free space varies inversely with the square of the distance and the pressure varies inversely with the distance from the source. Because the power is the product of the in-phase pressure and particle velocity, the relative magnitude of the particle velocity increases more rapidly than the pressure close to the source according to

$$u = \frac{p}{\rho c}\sqrt{1 + \left(\frac{c}{2\pi fr}\right)} \tag{3}$$

where f is the sound frequency. At a distance less than about 1/6 wavelength from the source, the particle velocity varies as $r^{-\frac{1}{2}}$.

As the particle velocity and pressure are not in phase, the air is behaving reactively close to a point source. This is of practical importance with small sources where most of the air load is reactive; for high acoustic efficiency, the source must be large enough for the loading to be resistive and this will be found only with sources whose diameter exceeds λ/π or about 1/3 wavelength (Fig. 1).

Below this size, the acoustic loading depends on whether the source is freely suspended or set in a baffle. For the freely suspended piston source, the resistance falls as radius^{-4} and with the piston in a baffle the resistance falls as radius^{-2}. Thus it is an advantage from the point of view of sound production efficiency if a source is placed in a baffle whose diameter exceeds $1/3\lambda$.

If the diameter of a flat piston source is larger than about λ/π the sound is radiated as a beam which becomes longer and narrower as the diameter of the disk increases. A freely suspended piston smaller than λ/π in diameter radiates from both sides and the sound distribution is a figure-of-eight whose long axis is normal to the disk. If the disk is surrounded by a baffle, the sound distribution on each side of the baffle is hemispherical with the disk at the centre.

It is evident from the critical examinations which have been made of several types of insect song that the types of transducers and the directional properties are closely related to the biological context in which they are used.

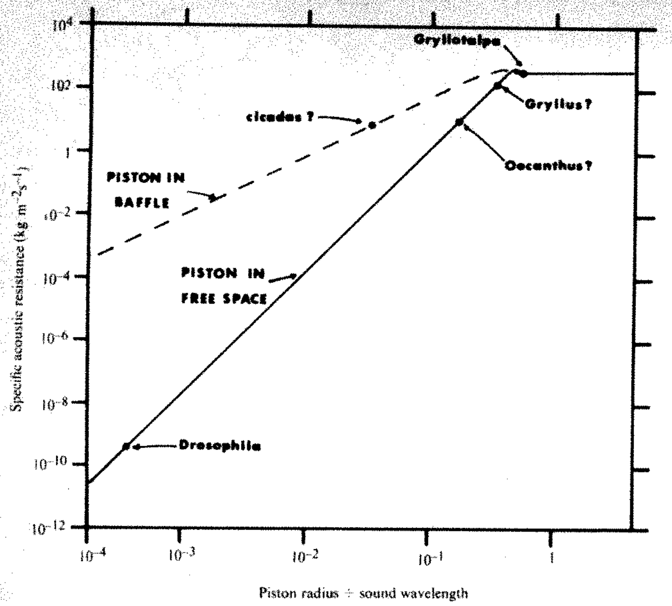

Fig. 1 Graph of the specific acoustic resistance against radius for two types of source. The curves are redrawn from ref. 2 and the points for *Drosophila* and *Gryllotalpa* are calculated from my data[12,26]; those for cicadas, *Oecanthus* and *Gryllus* are estimated from the size and type of transducer.

Insects' Hearing

Insects have many different types of auditory organ[3,4]. The simplest of these is the sensory hair which responds to displacement of the surrounding air. These receptors are found on the anal cerci and on other parts of the body and they have a low frequency response, giving a synchronous nervous discharge at frequencies up to about 300 Hz (ref. 5).

The antennae of many insects also respond to sound. In *Diptera*, the antennae are the principal organs of hearing and are tuned and directional. In the male mosquito, the antenna is most sensitive at the wing-beat frequency of the female[6,7] and, because the antenna does not vibrate along its axis when exposed to sound arriving from the side, indicates the direction of the source. In cyclorrhaphous flies the antenna bears a feathery arista which projects sideways from the apical joint; the arista can be displaced by the steady air flow or by the sound waves produced by the wings[8]. In *Drosophila*, the antennal arista can be set in vibration by sounds of 180 to 220 Hz and I have found that the amplitude of vibration is greatest when sounds arrive from 90° to the plane of the arista—about 30° away from the sagittal axis. There is mechanical and physiological evidence that the excitation of these receptors is by the particle displacement in the sound wave.

Higher frequencies can be received by tympanal organs; these are found in many groups, such as *Orthoptera*, *Homoptera* and *Lepidoptera*. There is a thin tympanal membrane on the body surface which is closely associated with internal tracheae or air sacs. Sensillae may be attached to the tympanic membrane or to the tracheae. The frequency response is usually from a few hundred Hz to more than 60 kHz and the nervous response is an asynchronous firing at the start or at the end of the sound pulse.

Frequency response curves for this type of receptor often show peak sensitivity to the song of the same species[9,10], and this may be due to excitation of specific neurones situated at antinodes of vibration of the tympanic membrane[11]; these different receptors in the locust are tuned with a Q of 3 to 6 and are thus able to discriminate between different frequencies and detect sound pulses of brief duration. Unfortunately no studies have yet been made of the mechanics of the tympanal organ in those insects that produce very pure single tones.

At one time it was thought that all insect hearing made use of displacement receptors. This arose because it was considered that the air sacs separating the two tympanal diaphragms were acoustically transparent. This view was reinforced by measurements which have the typical figure-of-eight directional response curve for the locust[3]; this was, however, probably produced with a mutilated insect. Michelsen[11] has recently examined the acoustics of the ear and air sacs in locusts and has shown that at the lowest frequencies, up to 5 kHz, the air sacs are effectively transparent and the response is probably to particle displacement. At higher frequencies from 5 to 15 kHz the impedance of the air sacs rises so the response is to the sound pressure; and because the body is of a substantial size, diffraction causes hearing to be unidirectional. At frequencies greater than 15 kHz, the acoustic load on the tympanum becomes significant and damps the natural resonances of the diaphragm; hearing is therefore not frequency sensitive.

The absolute sensitivity of hearing varies greatly, both with the insect and with the mechanism. Early work suggests thresholds of 50 to 70 dB for many species, including the locust[10]; these were measured on the basis of an obvious visible or audible record of the nervous discharge. If the threshold is defined in terms of the spontaneous nervous activity, during which the response is significantly greater over a period of time than the spontaneous response, it can be shown that the threshold level in locusts is some 40 dB less than the "all-or-nothing" threshold[11]. This absolute threshold may not be biologically significant because the duration of a steady state sound must be long if it is to be detected; most insect songs are made up of short pulses and can be recognized after as few as three pulses (A. W. Ewing and H. C. B.-C., to be published).

It appears that hearing in insects may discriminate the frequency, the intensity and the direction of the sound.

Very Small Insects

Many small insects such as some wasps, beetles and bugs produce sounds which are usually rather quiet. The general acoustic situation in such small animals can be analysed by using as an example the courtship song of *Drosophila melanogaster*—the waveform is fairly simple and the dimensions and amplitude of vibration of the sound producing organ are known[12].

During courtship, male *Drosophila* extend one wing towards the female and vibrate it, thus producing a series of sound pulses[13–15]. Each pulse is produced by a single beat of the wing which has a peak to peak amplitude of about 1 mm and period of about 6 ms (ref. 12). The wing is elliptical and has an area of about 1.25 mm². For the purposes of calculation of the acoustic power produced, the wing can be treated as a doublet source and the power is given by[2]

$$I=(2\pi fd)^2 r_M \qquad (4)$$

where I is the r.m.s. power in W, f is the frequency in Hz, d is the displacement in m and r_M is the acoustic resistance of the source in kg s^{-1}. For *Drosophila*, f is 166 Hz, d is 5×10^{-4} m, and r_M is the product of the area of one side of the wing, 1.25×10^{-6} m², and the specific resistance of a source whose effective radius is 3.0×10^{-4} times the wavelength of the sound (a resistance of 4×10^{-10} kg m^{-2} s^{-1} (Fig. 1)). The power radiated by each side of the wing is 1.3×10^{-16} W, which is too little to be heard directly.

The song must be related to the acoustics of the receptor which responds to particle displacement and is roughly tuned to the song frequency. During courtship, the male stands less than 5 mm (about 1/400 the sound wavelength) from the female fly. Sound pressure is distributed in a figure-of-eight pattern around a doublet source (Fig. 2) and, at a distance r, the isobar has an area πr^2. If the inverse square law was obeyed, as it is at values of r greater than about 1/3λ, the sound pressure would be 1.7×10^{-12} W m^{-2} or 2·5 dB. With a doublet source at a distance r less than about 1/6λ, the pressure is a factor of

$$\frac{\lambda}{2\pi r}$$

greater than this and the particle velocity is increased by a factor

$$\left(\frac{\lambda}{2\pi r}\right)^2$$

(ref. 2) which at 5 mm is 36 dB and 72 dB louder respectively. At 2.5 mm, which is rather more than the length of the fly, the calculated pressure is 51 dB above 2×10^{-5} N m^{-2} and the particle velocity is 95 dB above 0.5×10^{-7} m s^{-1} (Fig. 3.)

If a pressure sensitive microphone is used to record *Drosophila* song, elaborate sound insulation and high gain amplifiers are necessary[15]. But with a velocity sensitive microphone, no special sound insulation is needed in a noisy laboratory, and in experiments with artificial songs Ewing and I used pulses of 107 dB because lower powers were less reliable[17].

Flies stand on flat surfaces to court and the male fly faces the female. The courtship wingbeat is at 45° to the substrate[12] and this can be modelled using a small loudspeaker set close to a flat surface (Fig. 2). When the diaphragm is vertical, the distribution is the expected figure-of-eight. When the diaphragm is horizontal, the sound is quieter and non-directional in the plane of the surface. If the diaphragm is at 45°, the output is directed over an arc of 90° in the direction of squish; as the male fly orients himself roughly facing the female, he directs his song at her and other flies in the vicinity will not receive his song. This is important for a genus which tends to congregate on fruit or flowers.

From this study of *Drosophila*, it is clear that the displacement receptor is an advantage to animals which are very much smaller than the sound wavelength. Fish, for example, live in a medium with a high propagation velocity, 1,430 m s^{-1}, so the acoustic wavelength of their swimming or that of their food is many times the body length. Displacement receptors are used to monitor swimming or to catch food[18,19] but, at higher frequencies or over longer distances, fish use pressure receptors; moths also use these in the same way to hear the sonar cries of bats[20].

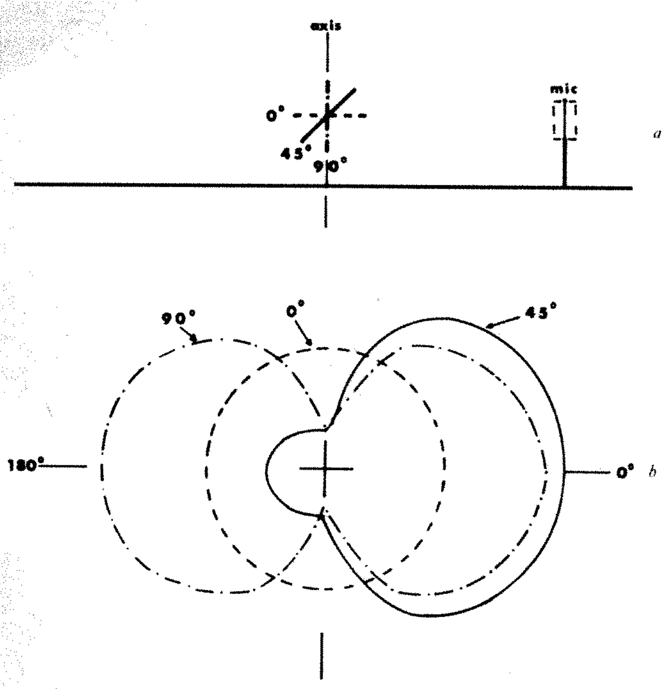

Fig. 2 Diagram of an acoustic model of *Drosophila* and its directional properties. *a*, A 50 mm diameter loudspeaker radiating 150 Hz is set 50 mm above a flat surface and 150 mm from a microphone, *mic*. The loudspeaker can be rotated about a vertical axis and the angle of the diaphragm to the surface can be altered. At 150 Hz, the sound wavelength is 2.25 m. *b*, Polar graph showing the relative sound pressure for different angles of the loudspeaker diaphragm to the surface. — · — · —, The diaphragm is vertical and the output is a figure-of-eight either side of the diaphragm; — — —, the diaphragm is horizontal and the output is non-directional; ———, the diaphragm is at 45° and the output is directed forwards and is maximal with the microphone in position *a*.

Large Insects

Many insects generate songs of remarkable noisiness. To produce these with maximum efficiency, a radiating surface with a radius larger than 1/6 λ is desirable and this restricts the frequency to more than about 3 kHz; a large number of insects, however, produce songs at more than 20 kHz. The songs of many insects have a dominant frequency and the energy spectrum is often narrow (Fig. 4); this suggests that the frequency is controlled by a part of the system that is not highly damped by the acoustic load and, because damping implies high conversion efficiency, the conversion efficiency may be low. Nevertheless, some of the loudest insects produce very pure songs.

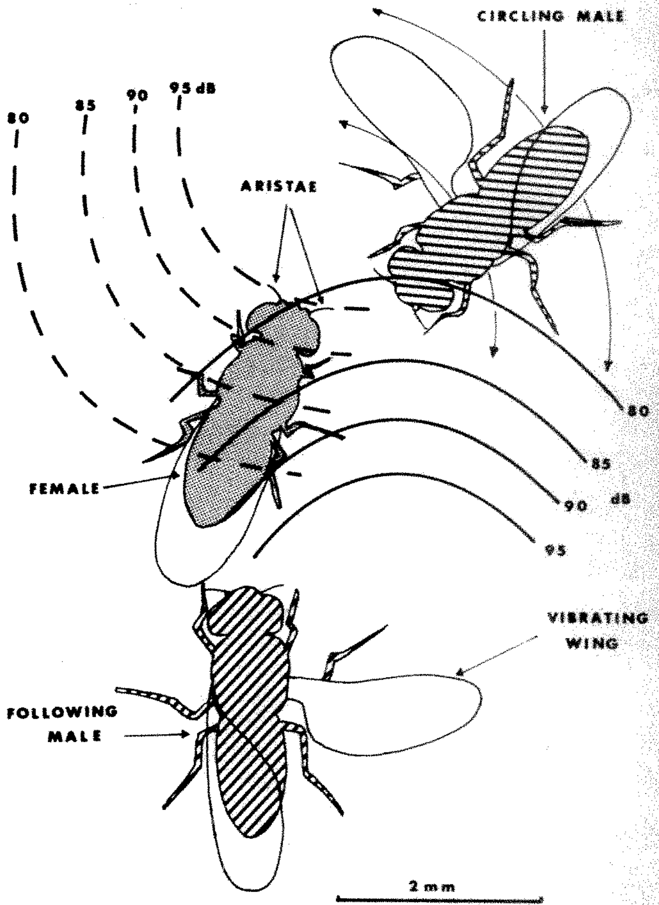

Fig. 3 Diagram showing the sound particle velocity produced by a male *Drosophila melanogaster* courting a female fly. The particle velocity contours are calculated and expressed in dB above 0.5×10^{-7} m s^{-1}.

Frequency Control

In most cases, the song frequency is determined by the resonance of either a disk or an elastic bar. The tymbal of cicadas[21] and the harp of field crickets[22] act as clamped disks excited in the case of cicadas by the periodic contraction of the tymbal muscles and in crickets by the passage of a plectrum over the file. The *Q* of the undamped disk of a cricket is about 25 but the mass of the air load damps this somewhat and the natural song has a bandwidth that suggests a *Q* of about 10 (Fig. 4).

The elastic bar is found in tettigonioids and mole crickets and vibrates at a frequency proportional to length^{-2} (refs. 23, 24). The resonance is excited by the passage of a plectrum over a toothed file but the type of song depends on whether the drop of the teeth on the file is synchronous with the primary resonance of the elastic bar. In most bush crickets, the resonance frequency is more than 10 kHz, and the closing stroke of the wings causes the plectrum to pass over 20 to 60 of the teeth on the file; at each drop of the tooth, a damped resonance of the bar occurs[25] and so the song is modulated first at the wing closing frequency and then at the tooth drop frequency. This type of song is usually impure, with a system Q of less than 5 and a broad frequency-energy spectrum (for example, *Phlugis* in Fig. 4).

If the bar is excited synchronously, the resonance is maintained and the frequency is very much purer (*Gryllotalpa* and *Drepanoxiphus*, Fig. 4); the song is modulated at the wing-closing frequency (up to 140 per second[24]). In this type of song the system Q is usually higher and the carrier frequency may be characteristic of the species and the range of individual variation; the bandwidth of an individual's song[26,27] suggests that the song carrier frequency may be of considerable biological importance.

The air load causes considerable damping of the vibration of the wing of a mole cricket and the song decays rapidly at the end of the pulse, suggesting a low Q resonator. The song is much purer than would be expected from such a system and this may be due to the considerable inertia of the dorsal field of the wing which will tend to cause the plectrum to drop the teeth on the file at a fairly constant rate; it is clear from records of the song at low temperature that the resonance of the elastic bar can be excited asynchronously and that the song is then far less pure[26]. Similarly, the examination of several tettigonioids suggests that the effect of altering the inertia of the wing[28] or of driving the wing at a rate not related to the song frequency is to produce an erratic pulse[29].

In summary, the song frequencies are determined by the excitation of some mechanical resonance but the purity of the song and the form of the pulse envelope may be affected by the way in which this excitation occurs.

Energetics of Singing

Acoustic measurements are difficult to make with precision and the fact that most insects do not remain stationary only complicates the problem. Mole crickets which sing from a burrow (Fig. 5) produce a pure song very regularly for a long period and it is therefore possible to measure the whole sound field and hence the total sound output. For *Gryllotalpa vineae* the output is about 1.2 mW with a peak level at 1 m of more than 90 dB. As the muscles responsible for the song only weigh about 50 mg and produce an estimated 3.5 mW, the efficiency is very high (about 35%, ref. 26). The small wings are placed across the horn-shaped burrow (Fig. 5) which provides a resistive load at the song frequency of 3.5 kHz. Examination of the size of the teeth and the area of the vibrating surface, the harp, suggests that the harp vibrates through about 125 μm.

If the harp is resistively loaded, the air mass can be calculated from

$$M_a = \frac{R_m}{2\pi f} \qquad (5)$$

where M_a is the air mass in kg, R_m is the acoustic resistance of the source in kg s^{-1} and f is the frequency in Hz. The area of the harp is 13 mm^2 and the air mass is about 0.25 mg. The mass of the membrane of the harp is about 0.35 mg and that of the veins surrounding the harp 0.8 mg, so the mass of the membrane and its air load are similar to that of the veins that drive it, which suggests a Q of less than 2. The mass of the dorsal field, however, is about 5 mg and, if this is considered to be the mass driving the resonant system, the system Q is given by

$$Q = \frac{\text{driving mass}}{\text{air load} + \text{membrane mass}}$$

This yields a value of 8.5. Considering the mass of the whole wing (12 mg) Q is 20. The measured Q is, in fact, about 16 (Fig. 4) so this explanation of the mechanism is a possible one. It would be useful to know the effects of altering the inertia of the wings or the compliance of the various parts of the system.

Although the energetics of *Gryllotalpa* song are probably the simplest to examine, other systems can also be studied; the tree crickets of the Oecanthinae produce very pure songs at about 2 to 3 kHz and hold the wings vertical while singing, making a doublet source. Pasquinelly and Busnel's measurements of the sound level of 68 dB at 10 cm (ref. 25) give a total power of 1.2×10^{-7} W. In this genus the area of the harp is about 15 mm^2 for both wings so the power output for a radiator of this size

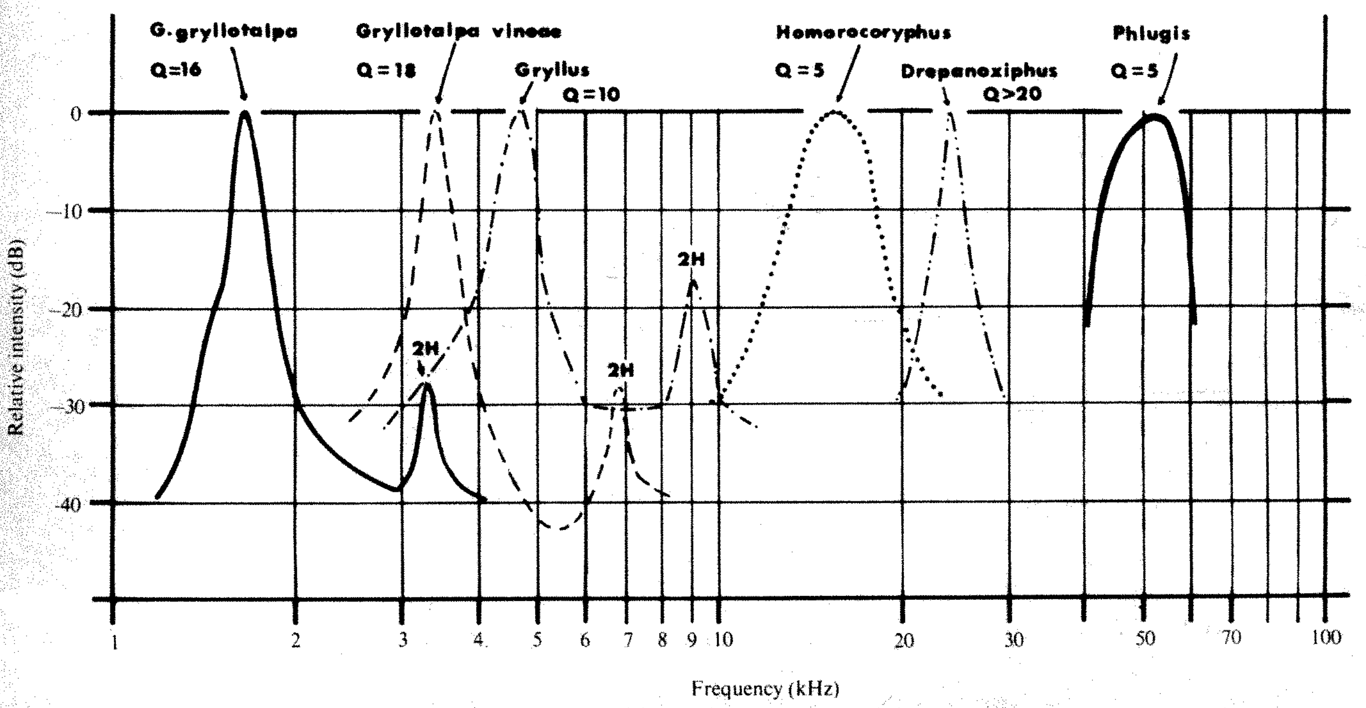

Fig. 4 Frequency-power spectra for various insects expressed as dB below peak level. The curves show the second harmonic content, 2H, and the Q has been calculated from the bandwidth at 3 dB below the peak. Data for *Gryllotalpa* and *Gryllus* are original, for *Homorocoryphys* from Bailey[24], for *Drepanoxiphus* and *Phlugis* from Suga[28].

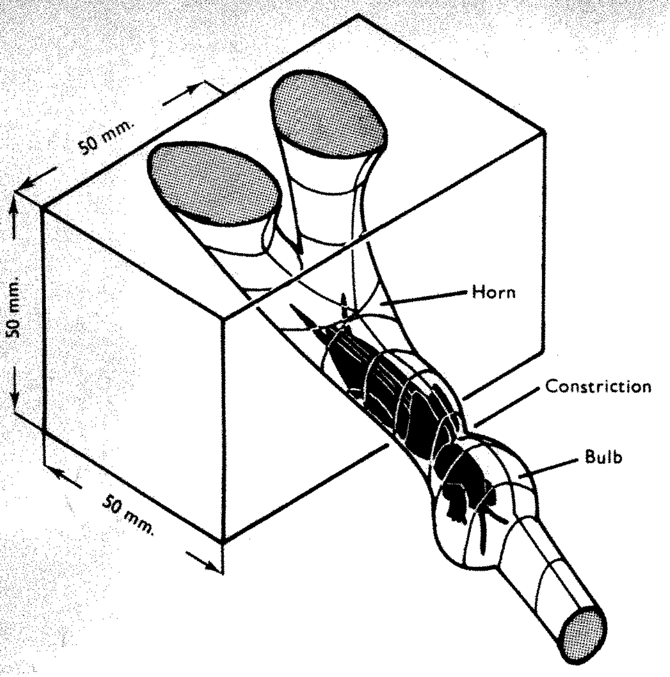

Fig. 5 Isometric drawing of the horn shaped burrow of *Gryllotalpa vineae*[26]. The horn provides a resistive load to the small wings of the insect, the bulb tunes the horn throat reactance and the two openings at the surface produce a disk shaped beam of sound.

(Fig. 1) is produced by a vibration of amplitude 7.5 to 10 μm (equation (4)) which is compatible with the dimensions of the file. The sound power is 40 dB less than that of *Gryllotalpa vineae* and Morse[30] has written of it that "if moonlight could be heard, it would sound like that". The biological value of such a low song intensity is not clear but the wavelength, about 15 cm, is less likely to be diffracted by such things as leaves than the 1 to 3 cm sound waves of bush crickets and so direction finding at close range may be better.

Field crickets of the Gryllinae make far louder sounds than Oecanthinae and a power output of about 6×10^{-5} W has been estimated[26]. The song wavelength is about half that in *Oecanthus* so the specific radiation resistance is about 16 times greater and, because the lateral fields of the wings are held against the side of the body, the effective diameter of the source is much increased. The result is that the radiation resistance is many times that in *Oecanthus* but still far less than that in *Gryllotalpa* in its burrow. The efficiency of sound production is estimated at about 5%. Acoustically, cicadas can be regarded as a pair of small transducers in an infinite baffle[31]. The resonance of the tymbal is not very highly damped (though this has not been measured) and this is consistent with a system in which the acoustic loading is not very high (Fig. 1).

It should be possible to offer a fairly precise description of the acoustic transducer but so far this has only been done in the simplest cases.

Output Directionality

In most biological contexts it is an advantage to direct the sound output. For a given sound output, a directional beam will have a greater range than the same power distributed equally in all directions.

If the sound is produced by a displacement transducer or a doublet source, the output is a figure-of-eight (Fig. 2) but the distribution is affected by proximity to the substrate and the form of the transducer. Nöcke has shown that *Gryllus* sound is produced from a modified doublet source and that the sound is loud behind the insect but that there is a null at right angles to the sagittal plane[22]. This directionality is partly due to the angle at which the wings are held and partly to the substrate; the effect is that the insect can turn and direct a beam of sound close to ground level. Similar effects probably occur with *Ephippiger* but here the song is directed backwards and to one side by the pronotum and abdomen[25].

With a small pressure transducer, the sound output is non-directional but the shape of the surroundings may be important. Aidley has shown that cicadas produce a maximum intensity either side of the sagittal plane which can be related to the diffraction of sound by the body of the insect and the position of the tymbals[31]. In mole crickets, the horn can be regarded as a large pressure transducer set in a flat baffle and has two mouths each about $1/3\ \lambda$ in diameter and about $1/3\ \lambda$ apart. The calculated response for a source of size about $0.6\ \lambda$ by $0.3\ \lambda$ is a semicircular disk shaped beam normal to the long axis of the source and the measured sound distribution is similar to this[26]. The advantage is that the surface area of such a beam viewed parallel to the ground is larger than that of a hemisphere of the same total surface area and this would be about 1.4 times as effective in attracting horizontally flying insects as the same power radiated equally in all directions.

The Complete System

Although much is known of the behavioural context of different types of songs in many different species, very few studies have been made of the acoustics of both the sound producing and sound receiving organs in the species and these have not so far been sufficiently rigorous. Little, for example, is known of the directional properties and acoustics of field cricket hearing, nor is much known of the acoustics of sound production in locusts. In my speculative examination of the acoustics of *Drosophila*, I have endeavoured to show that it is only valid biologically to consider sound production as it is related to the context and the acoustics of each end of the system.

I thank Dr G. T. R. Done for assistance with some of the mechanics and Dr H. Nöcke for discussing his work before its recent publication. I have not, at the time of writing, been able to obtain his paper.

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Absolute Gamma-ray Dosimetry by Recoil Electron Spectroscopy

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The difficulties associated with the measurement of continuous gamma-ray spectra can be overcome by a new absolute dosimetry method which does not require the use of other detectors or of radiation standards.

We have developed a new method of absolute gamma-ray dosimetry which is based on recent work in Compton recoil gamma-ray spectroscopy[1,2] and which properly accounts for the most fundamental quantity in the specification of a gamma-radiation field, namely the absolute gamma-ray energy spectrum. The sensitivity of the method is of particular importance in radiation biology and environmental science[3-4].

Continuum Spectroscopy

The large number of types of gamma-ray spectrometers that already exist determine gamma-ray energies of discrete line spectra. But the inability of these spectrometers to distinguish easily between photoelectric and Compton scattering events precludes measurement of continuous spectra. Suppression of Compton scattering requires detectors whose size and/or density perturbs the gamma-ray spectrum because of scattering in the detector material itself. In detectors of low atomic number, however, Compton scattering predominates for a broad gamma-ray energy range. For example, in lithium-drifted silicon detectors, which have been used in Compton-recoil gamma-ray spectroscopy, Compton scattering dominates all other types of interactions for gamma-ray energies from 0.2 MeV to ~3.0 MeV. For plastic and liquid scintillators such as stilbene and xylene, Compton scattering dominates over an even greater energy region—from 0.02 MeV to ~5.0 MeV.

Although the correspondence between the gamma-ray energy spectrum and the resultant Compton electron energy spectrum is not uniquely one-to-one, it can be represented by

$$W(E) = N_e \int \frac{d\sigma_c}{dE}(E,\varepsilon)\, \Phi(\varepsilon)\, d\varepsilon \qquad (1)$$

where $W(E)$ is the Compton distribution of recoil electrons per unit time and $\Phi(\varepsilon)$ is the gamma flux energy spectrum. The kernel

$$\frac{d\sigma_c}{dE}(E,\varepsilon)$$

of this integral equation is the Compton cross-section per free electron, scaled by N_e, the total number of electrons in the detector. The Compton cross-section may be obtained from the Klein–Nishina formula and equation (1) may then be unfolded to determine the gamma-ray energy spectrum, $\Phi(\varepsilon)$.

We have used a lithium-drifted silicon detector 2.0 cm^2 by 0.5 cm depletion depth, mounted in a light aluminium vacuum chamber, to measure the induced Compton recoil electron spectra of unknown gamma radiation fields. The detector assembly produces very little perturbation of the gamma-ray spectrum and output pulses due to Compton electrons that are totally absorbed within the detector are sorted and the information stored in a multi-channel analyser; pulses caused by Compton electrons that enter or leave the detector are electronically rejected. These so called wall events interact in the dead regions of the solid state detector, where the weak fringing field produces relatively slow charge collection. Consequently, wall events in these solid-state detectors possess much slower rise times and can therefore be rejected using pulse-shape discrimination[1]. Finite detector size corrections are used but these become unreliable at about 2.2 MeV for this particular silicon detector.

Now $W(E)/N_e$ represents the $\Phi(\varepsilon)$ induced Compton electron distribution per free electron within the silicon detector and, within other materials of low atomic number, an identical Compton electron distribution per free electron will be induced by $\Phi(\varepsilon)$ provided that the amount of material does not perturb the gamma-ray spectrum and that electronic equilibrium has been established within the material (thus precluding from consideration a surface region of thickness equal to the range of the Compton electrons). The fundamental quantity, $W_{IM}(E) = W(E)/N_e$, will therefore be referred to as the infinite medium Compton electron spectrum per free electron.

Scintillators

Many of the same considerations which have been applied to the lithium-drifted silicon detector can also be applied to the use of conventional liquid and plastic scintillators in which Compton response predominates. The rejection of defective events caused by recoil electrons which leave the scintillator is, however, not easily amenable to experimental treatment as it is in the silicon detector. There is at least one alternative solution to the problem of electronic non-equilibrium. Because the problem is essentially a surface effect, it can be minimized by choosing larger scintillators with higher volume-to-surface ratios; increasing the scintillator size, however, increases the probability of multiple Compton interactions. This new problem can be viewed in several ways. The presence of the larger detector perturbs the gamma-ray spectrum such that the gamma field inside the detector is quite different from the external field. If each individual Compton interaction could be detected by an individual scintillation, the resultant Compton electron spectrum could be unfolded by the simple application of equation (1) to establish the average internal gamma-ray energy spectrum. Unfortunately it is not possible to separate individual scintillations due to multiple Compton interactions. Thus, for example, a multiply scattered 4.0 MeV gamma-ray that successively induces two Compton-recoil electrons of 1.0 MeV and 2.0 MeV in a scintillator will produce only a single response corresponding to an energy deposition of roughly 3.0 MeV. By contrast with solid state silicon detectors, which require finite size corrections, one must consider multiple scattering effects in continuous gamma-ray spectroscopy with large scintillators. And by analogy with the treatment of finite size effects, a correction factor would be introduced into the kernel of equation (1). This factor can be experimentally determined through the use of mono-energetic gamma-ray sources or it can be calculated by Monte Carlo methods. Once this multiple scattering factor is established for a particular scintillator, equation (1) can be used to determine the external gamma-ray energy spectrum.

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On the basis of this work, it may also be possible to determine the internal gamma-ray spectrum, that is, the spectrum which exists within the detector. Although the determination of either the external or the internal gamma-ray spectrum is subject to multiple scattering corrections, the nature of these corrections is quite different in each case. The influence of multiple scattering can be eliminated during the unfolding of the internal electron recoil spectrum to obtain the external gamma-ray spectrum. To obtain the internal gamma-ray spectrum, however, corrections must be introduced to "resolve" the multiple scattered recoil electrons that are a component of the internal Compton recoil spectrum. It is the internal gamma-ray spectrum and the corresponding induced Compton recoil spectrum which are of substantial interest in radiobiology.

The most attractive advantage of scintillators for use in gamma-ray spectroscopy is the high event rate possible with larger detectors. A 12.7 cm diameter sphere of liquid scintillator gathers data about 300 times faster than the silicon detector described above. Consequently, any disadvantages arising from the required multiple scattering correction and the broader resolution of the scintillator are counterbalanced by the great improvement in statistical precision of the observed Compton electron continuum.

Absolute Dosimetry

In materials of low atomic number, the gamma-ray spectrum induces a unique Compton recoil continuum which provides, in turn, the direct mechanism for gamma-ray energy deposition. The infinite medium dose rate $\dot{D}_{\mathrm{IM}}$ or, equivalently, the energy deposited per unit time and per unit mass by $W_{\mathrm{IM}}(E)$ in a material of low atomic number with electron density ρ (electrons per unit mass) is

$$\dot{D}_{\mathrm{IM}} = \rho \int E \cdot W_{\mathrm{IM}}(E) \mathrm{d}E \qquad (2)$$

Although equation (2) is only valid for infinite medium spectra, an immediate generalization is possible. The general relation between dose rate $\dot{D}$, and the recoil electron spectrum $W(E)$ can analogously be written as

$$\dot{D} = \rho \int E \cdot W(E) \mathrm{d}E \qquad (3)$$

where $W(E)$ is the actual recoil spectrum—measured in a silicon detector or a plastic or liquid scintillator—which can therefore include both finite size and multiple scattering effects. It follows that the dose rates based on equation (3) will automatically account for these effects. The infinite medium dose rate, $\dot{D}_{\mathrm{IM}}$, of equation (2) represents a point dose rate value and so corresponds to an absorbed dose rate without perturbation of the gamma-ray spectrum. On the other hand, the dose rate $\dot{D}$ obtained from equation (3) properly accounts for the effects of the absorber on the external spectrum.

The fundamental advantage of the new approach must be stressed. By contrast with other methods it is clear that dose measurements based on equation (2) or equation (3) automatically account for the continuous energy distribution of the gamma-ray field. The absolute nature of these measurements depends intimately on the energy calibration of the electron spectrum. The correlation between detector response and electron energy may be accomplished in several ways but does not require a gamma source of known intensity. A mono-energetic gamma source is, for example, sufficient to determine the correlation.

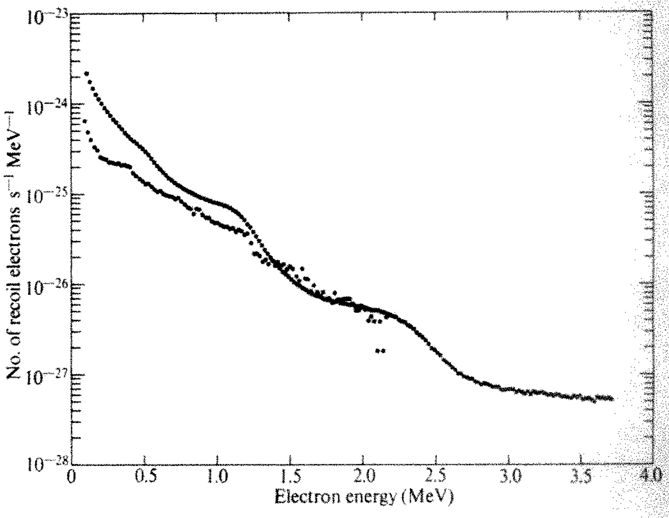

Fig. 1 Environmental electron recoil spectra observed at the Argonne National Laboratory site with a silicon solid state detector (lower curve) and a large liquid scintillator (upper curve). Each spectrum represents number of Compton recoil electrons per second per MeV and per detector electron.

Both the lithium-drifted silicon detector and the scintillators possess unique advantages for dose measurements. The silicon detector can be used for point dose measurements, but, on the other hand, the scintillators are inexpensive and can be formed to study average dose in specialized configurations. And by varying the proportional size of the scintillator, surface-to-volume effects can be studied. The two classes of detectors can be used together to investigate multiple interactions and the fundamental distribution of dose. The high sensitivity of the large scintillators makes them quite attractive for environmental measurements and particularly for the development of isodose curves.

Measured Spectra

The induced Compton recoil spectra of two complementary detectors, a 12.7 cm diameter sphere of NE-213 (Nuclear Enterprises, Inc.) liquid scintillator (~ 10^3 cm^3) and a lithium-drifted solid state silicon detector (~ 1 cm^3), are shown in Fig. 1. Both spectra represent environmental measurements made at the Argonne National Laboratory site. The recoil electron spectrum in silicon was recorded in March 1970 and the spectrum in the scintillator was recorded in April 1971. In each spectrum, a Compton edge at 1.245 MeV due to the 1.461 MeV gamma emission of potassium-40 is apparent. The scintillator spectrum also displays a Compton edge at 2.38 MeV due to the 2.615 MeV gamma emission in the thorium series. The structure of the scintillator spectrum clearly lacks the resolution of the lithium-drifted silicon electron spectrum. But the broader resolution of the scintillator

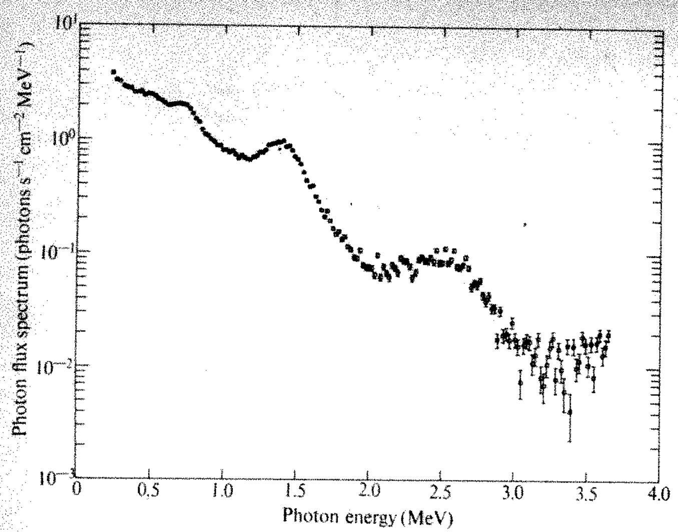

Fig. 2 Environmental gamma-ray spectrum measured by Compton recoil electron spectroscopy with a 12.7 cm diameter liquid scintillator at the air–land interface.

is partially compensated by the improved statistical accuracy available because of its greater size.

The energy scale of the silicon spectrum presented in Fig. 1 has been established with a caesium-137 gamma source. In silicon, there is sufficient photoelectric response to detect a photopeak at 0.661 MeV. No photopeaks due to mono-energetic gamma-ray sources are apparent in the response spectrum of the liquid scintillator because of the reduced photoelectric effect and the broader resolution of the scintillator; the energies of the Compton edges from laboratory sources of zinc-65, sodium-22 and tellurium-208 were therefore used. The calibration procedure involves the convolution of a calculated Compton electron distribution with a Gaussian broadening factor. Energy and broadening parameters are adjusted to obtain the best least-squares fit between the measured electron recoil spectrum and the convoluted distribution. An agreement of 4.0% was obtained among the energy calibrations determined with these three different gamma-ray sources.

Fig. 2 represents a continuous gamma-ray spectrum unfolded by the direct application of equation (1) to the scintillator electron recoil spectrum of Fig. 1. The 1.461 MeV gamma emission of potassium-40 and the 2.615 MeV gamma emission in the thorium series are properly located in photon-energy space and this implies that proper calibration has been obtained in electron energy space. Even though no corrections were applied for multiple scattering, the spectral results shown in Fig. 2 are in qualitative agreement with environmental spectra determined with the silicon detector[3,4].

Environmental dose rates have been obtained from the electron spectra in Fig. 1. A point dose rate of 4.3 ± 0.9 μR h^{-1} was observed with the silicon detector in the gamma-ray energy region 0.2 MeV to 2.2 MeV whereas a gamma dose rate of 3.0 ± 0.3 μR h^{-1} was observed with the scintillator in the gamma-ray energy region 0.2 MeV to 3.0 MeV. The dose rate observed with the scintillator is almost unchanged if the data are restructured to correspond to the gamma-ray energy range of the silicon detector. Although the two dose rates are barely outside experimental error, no agreement is implied because the two experiments were carried out at times separated by many months. It is anyway expected that the dose rate results would differ for these two detectors because the size of the scintillator can produce a perturbation of the environmental gamma-ray field.

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Selective Volatilization on the Lunar Surface: Evidence from Apollo 14 Feldspar-Phyric Basalts

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Analysis of Apollo 14 samples has revealed a basalt that could be parental to the highlands anorthosites.

One of the most strongly contested arguments among scientists investigating the chemistry of lunar rocks is the cause of their low content of volatile elements. In particular, the mare basaltic lavas are notably depleted in sodium and potassium compared with otherwise equivalent terrestrial basalts[1,2]. The three hypotheses at present are (1) the Moon was volatile-deficient at the accretionary stage, due either to higher peripheral temperatures or to a lower accretion efficiency than the Earth[3,4]; (2) certain elements, including K and Rb, became concentrated at an early stage in a sulphur-bearing core[5]; (3) volatiles were lost from the lavas during eruption and flow in the low-pressure environment of the lunar surface[6,7].

A second important problem concerns the nature and origin of the Moon's crust. If, as seems likely, this is an anorthosite[8] there are serious problems in finding a source for this material among the mare basalts. To obtain such a monomineralic rock (melting temperature 1,530° C) requires feldspar accumulation from a lower temperature (1,100 to 1,200° C) basalt magma. The Apollo 11 and 12 basalts failed, however, to show textural or experimentally derived evidence for a feldspar phase on the liquidus. Associated with this problem is the europium anomaly in the basalts, which suggests that plagioclase feldspar (carrying Eu^{2+}) did, in fact, separate from more primitive basalts with normal rare-earth abundance patterns. Thus the question that arises is whether the primitive lunar crust was derived from a more aluminous basalt than that collected from the mare regions and, therefore, whether the accretion of the Moon produced a layered structure from which basalts of differing composition could be generated at differing times and depths. A third problem is whether the sampled lavas are derived directly from the lunar mantle or whether they have suffered crystal differentiation near the lunar surface.

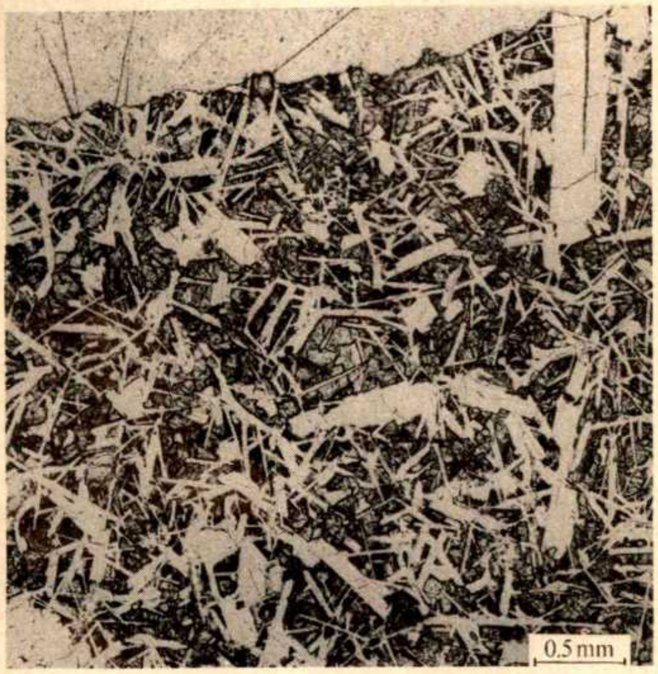

Fig. 1 Photomicrograph of feldspar-phyric lunar basalt (14310/20). The separate generations of rectangular plagioclase feldspar phenocrysts (colourless) and criss-cross laths of groundmass plagioclase are clearly visible. The laths are intergrown chiefly with Ca-poor pyroxene.

Fra Mauro Specimens

We have been studying basalt specimens from the recently allocated suite of Apollo 14 specimens, collected from the Fra Mauro formation. Unfortunately, apart from a preliminary report[9], little information has yet been published on this suite. We cannot, therefore, carry our conclusions as far as we would wish in the absence of refined data on whole-rock compositions, europium contents and the model and isochron ages of the rocks we have examined. Even so, we have obtained information which goes some way to answering the problems mentioned previously and which raises new questions on several lunar geochemical and evolutionary topics.

First, the two basalts received from Houston (14310 and 14073) are each clearly feldspar-phyric (for example, Fig. 1) and are the first lunar basalts to show this property. Also, they are much richer in total plagioclase feldspar (average 53%) than the Apollo 11 and 12 basalts (25 to 40%), as evidenced by the Al_2O_3 content of 14310 (20% by weight[9]). This rock is also much richer[9] in K and Rb than the "high K" basalts of Apollo 11. It is safe to assume that with such a composition and with about 10% of large phenocrysts, plagioclase crystallized on or very close to the liquidus. Such a basalt could produce anorthosite by floating of the phenocrysts but, if so, it should not, in the undifferentiated state, show the full europium anomaly characteristic of the plagioclase-depleted mare basalts.

Table 1 Plagioclase Feldspar Compositions by Electron Probe Analysis

Specimen	Crystal generation*	Ca/ (Ca+Na+K) atomic %	Na_2O wt %	K_2O wt %
14310/13	PC	91.5	0.91	0.09
	PI	85.5	1.52	0.25
	PR	75.4	2.42	0.52
	PC	92.5	0.77	0.12
	PI	90.0	1.04	0.13
	PR	87.0	1.29	0.25
	PC	95.0	0.51	0.08
	PI	93.5	0.64	0.15
	PR	86.0	1.42	0.27
	GL	94.5	0.51	0.15
	GML	91.0	0.77	0.35
	GML	92.5	0.77	0.15
14310/20	P	90.5	1.00	0.14
	P	90.0	1.06	0.12
	P	91.5	0.86	0.14
	P	91.5	0.86	0.12
	GL	93.0	0.73	0.14
14073/9	PC	93.0	0.73	0.09
	PI	91.5	0.86	0.13
	PI	88.0	1.21	0.21
	PR	72.5	2.67	0.59
	PC	93.0	0.73	0.13
	PI	85.0	1.45	0.39
	PR	67.0	3.14	0.73
	PC	91.5	0.86	0.13
	PI	87.0	1.34	0.19
	PR	86.5	1.34	0.21
	GL	94.0	0.61	0.13
	GML	91.5	0.86	0.15
	GML	94.0	0.61	0.09

* P, Apparently unzoned phenocryst; PC, zoned phenocryst core; PI, zoned phenocryst intermediate sheath; PR, zoned phenocryst rim; GL, groundmass lath (unzoned); GML, groundmass microlath in residual mesostasis.

Analyst: A. Peckett.

Second, we have analysed thirty crystals of plagioclase (Table 1) by electron probe analysis (performed by A. P.) in three polished rock sections—14310/13, 14310/20 and 14073/9. There are several generations, with contrasted compositions. Briefly, the phenocrysts are strongly zoned to more sodic and potassic compositions whereas the abundant groundmass laths (Fig. 1), and even the micro-laths in the residual mesostasis, are as low in sodium and potassium as the phenocryst cores. In view of these data, we propose that the basalt lavas lost Na and K on the lunar surface. Also, we propose that the lavas were erupted in two stages, the first of which would permit appreciable, near-surface crystallization differentiation of once-primitive lavas. As far as selective volatilization is concerned, we must question whether analyses of surface-erupted lunar basalts can be used to postulate a unique, alkali-poor composition for the whole Moon.

Specimen 14310 is from a 3.4 kg basalt block, and 14073 is a soil fragment from the base of a 60 cm deep trench (both Station G)[9].

Analytical Data

Modal point-counts are not particularly accurate, so we can only propose a plagioclase content, for 14310/20 (Fig. 1), of $53\pm3\%$; the possible error does not influence the subsequent argument. Even more difficult is the calculation of the phenocryst core plus rim contents, which we estimate to be 10%. The remaining 43% of plagioclase is present as groundmass laths, producing the dominating ophitic texture with Ca-poor pyroxene (Figs. 1, 2) and as small patches of micro-laths in a residual mesostasis (Fig. 3). The last of these includes $\leqslant 1\%$ of analysed barian sanidine and potassic rhyolite glass which are used in the K-content calculations (Table 2). Otherwise the rock contains relatively small amounts of the phases that we have found in other Apollo basalts (nickeliferous iron, troilite, ulvöspinel, ilmenite, pyroxferroite, whitlockite, baddeleyite) but no olivine or cristobalite and very little calcic pyroxene and chrome-spinel.

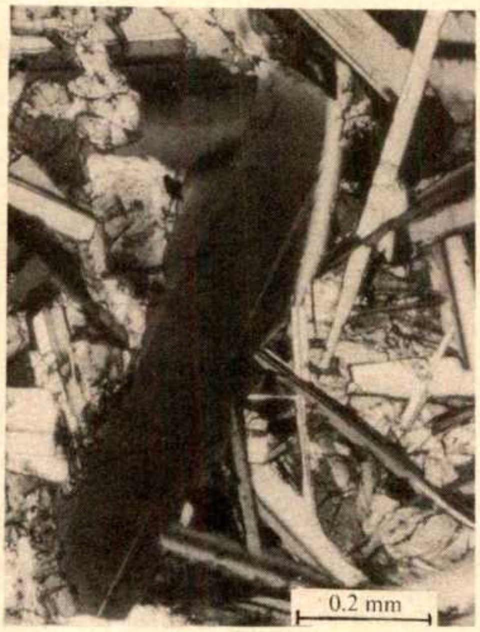

Fig. 2 Photomicrograph showing normal zoning of large plagioclase phenocryst, which has a sodic rim (14310/13). Groundmass of calcic plagioclase laths and pyroxene, the laths being discontinuous with the phenocryst rim. Crossed polars.

The plagioclase analyses are reduced simply to "anorthite" values (atomic Ca/(Ca+Na+K)) and the weight percentages of Na_2O and K_2O (Table 1). Because of possible criticisms of generalized data, we have given the data for all analysed grains.

There are no notable exceptions to the following conclusions. The phenocrysts have large, homogeneous cores as calcic as Ca95, with a mean value of Ca94. Most phenocrysts have a discontinuity between core and rim, the rims being zoned continuously (Fig. 2) as low as Ca67 in one instance. (It is not possible to detect and measure extreme compositional trends on all the outermost rims.) We can safely assume, however, that the magma was only capable of precipitating material of a less calcic composition than Ca67 at the phenocryst rim stage. In marked contrast, the abundant, groundmass plagioclase crystals (Fig. 3) are much more calcic than the phenocryst rims. The measured range is Ca94.5 to Ca91 (the latter being potassic rather than sodic), for which we take a grain-number mean of Ca93. The values are given as Ca% for convenience, but the significance lies in the associated pattern of distribution of Na_2O and K_2O (Table 1). In cases where the amounts of these two oxides are small, experimental error reduces the significance of minor differences. We note, but do not use in the calculations, a mean value of 0.61% Na_2O and 0.12% K_2O for the phenocryst cores (Ca94). For the phenocryst rims, we must take the most sodi-potassic example analysed (Ca67) because this represents the minimum range of zoning. For this rim, the values are 3.14% Na_2O and 0.73% K_2O. Finally, the calcic groundmass laths average at Ca93, with 0.70% Na_2O and 0.13% K_2O. There is no significant difference between these and the phenocryst cores. Also, the same pattern of reversal would arise from the selection of any triplet (core, rim, lath) from Table 1.

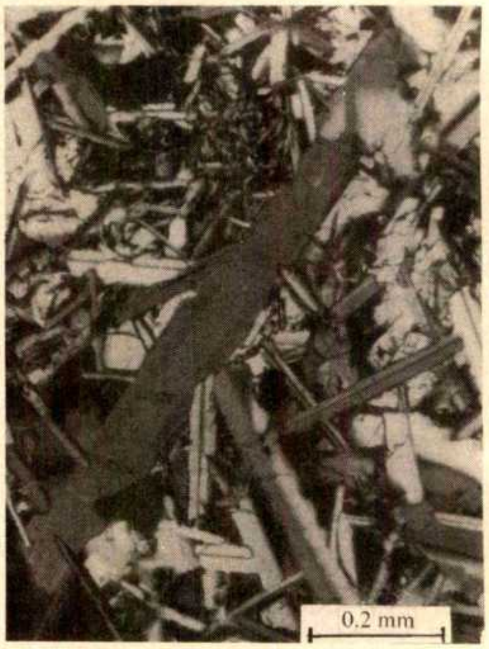

Fig. 3 Photomicrograph showing three generations of plagioclase feldspar (14310/13). A small, normally zoned phenocryst (centre); abundant, calcic groundmass laths; and a residuum area with calcic micro-laths (top centre). Crossed polars.

Alkali Loss

The normal zoning of the calcic plagioclase phenocrysts to Ca67 leads to the assumption that, under normal magmatic conditions, the groundmass plagioclase would be at least of the same composition. Certainly it could not, according to phase relations in the system An-Ab-Or, be more calcic and poorer in Na and K. As we have seen, however, the Apollo 14 basalts show abundant groundmass plagioclase crystals with this property. In place of the normal cooling process of a closed system, the only mechanism likely to produce such a drastic effect would be the loss of Na and K from the system at this stage. Non-equilibrium, rapid cooling of a closed-system magma would still have produced a less calcic plagioclase than that of the phenocryst rims.

A very conservative estimate of the alkali loss is shown in Table 2. The unknown factor is the "potential plagioclase" in the magma before loss of volatiles, and we have therefore retained a known, minimum value in terms of Na_2O and K_2O content. We can estimate with some certainty, however, the normative plagioclase in a liquid that had just precipitated the Ca67 (or An67) rims to the phenocrysts. From the simple synthetic system An-Ab, the normative liquid plagioclase would be An26. More closely, from natural polycomponent systems, the liquids from which plagioclases have crystallized in equilibrium have been calculated in a layered intrusion[10]. These show An67 in equilibrium with An56 liquid. The "liquid" analysis[10], recalculated in terms of its plagioclase content, shows about 5% Na_2O, and most published analyses of An56 crystals indicate about 8% Na_2O. The K_2O values are too low to be significantly altered by this refinement. The value of 3.14% Na_2O in Table 2 could legitimately be increased by a factor of 2, and the value for K_2O could probably be increased by a factor of about 1.5, strengthening the argument concerning alkali loss even further. This potential plagioclase in the liquid would, of course, crystallize as more than one phase (sodic plagioclase, potassic feldspar, and possibly a syenitic residual glass) as the temperature dropped.

Table 2 Calculation of Alkali Loss during Volatilization

	Phase	Vol. % in magma/rock*	Na_2O (wt%)	K_2O (wt%)
Before volatile loss	Potential plagioclase, Ca67	44%	3.14	0.73
After volatile loss	Groundmass plagioclase, Ca93	43%	0.70	0.13
	K-feldspar (K_2O=13%)	0.5% max.	0.00(5)	0.06(5)
	K-rhyolite (K_2O=7%)	0.5% max.	0.00(4)	0.03(5)
	Total of three phases		0.80	0.23
Volatile weight loss			2.34	0.50
% loss from original			74	68

* Modal volume used only for calculating relative contribution of the three phases analysed in the rock. The "potential plagioclase" is equated with the extreme, analysed phenocryst rim (Table 1) and would be an under-estimate of original, potential Na_2O and K_2O. Percentage losses are therefore likely to have been even greater than calculated.

The minimum values calculated in Table 2 show that the loss of Na and K has been appreciable, amounting to 74% Na_2O and 68% K_2O loss. Using the refinement outlined above, these values would be 86% Na_2O and 78% K_2O.

An experimental study of selective volatilization has been carried out by G. M. Biggar (personal communication). He used a terrestrial basaltic rock (Scourie dyke, iron-rich tholeiite) as the starting material, at $fO_2=10^{-12}$ bar and with original contents of 2.38% Na_2O, 0.92% K_2O. There was appreciable loss of these oxides and, in extreme cases, depletion to 0.13% Na_2O, 0.12% K_2O occurred. Close comparison with our observations is possible for less extreme experiments which show 75% loss of Na_2O and 73% loss of K_2O (compare Table 2). These losses occurred during experimental runs of 24 to 60 h at 1,160 to 1,175° C and at pressures between 1.5×10^{-4} and 2×10^{-5} torr.

It follows that the conditions on the lunar surface, where basalt magmas were erupted at about 1,100 to 1,200° C in an atmosphere with a pressure of the order of 10^{-12} torr, would be appropriate for alkali loss during flow for 1 or 2 days.

Pyroxenes

The plagioclase-phyric basalts contain abundant pyroxene (Fig. 1), most of which has crystallized ophitically with the small calcic plagioclase laths. Small cores to each pyroxene may, however, have crystallized before volatile loss. These cores are the lowest in Ca and highest in Mg of any lunar pyroxene so far analysed from a basalt. They are close to Ca3 Mg81 Fe16 and zone outwards to more iron-rich pigeonites, and eventually through subcalcic augite to pyroxferroite. Hence the Apollo 14 pyroxenes are more primitive pyroxenes than those found in Apollo 12 basalts, which in turn were more primitive (pigeonite-rich) than those in the Apollo 11 basalts. The more magnesian character of the Apollo 14 pyroxenes is more closely comparable with those in the norite fragments[11] from the regolith at all three sites than with the mare basalts. Perhaps the specimens under discussion should be called norites; if so, they provide better textural evidence for a magma of this type than has so far been obtained from the frequently shocked regolith fragments[12]. They also show, in their late pyroxene trends and in the character and texture of the KREEP residual material, close analogy with the crystallization trends in the Apollo 12 mare basalts[11]. The pyroxenes are less aluminous than in the mare basalts, probably because of co-precipitation with abundant early plagioclase. The Al:Ti ratios are very high (up to 7:1), despite their low-pressure crystallization, indicating a low Ti activity for these aluminous basalt liquids. Soil fragments at the Apollo 14 site have been found to contain similarly magnesian orthopyroxenes to those in the feldspar-phyric basalts (Ca3 Mg81 Fe16). Some also contain olivine of Mg90 Fe10, indicating a minimum lunar mantle composition of Mg/(Mg+Fe)=0.9.

Two-stage Process

The lunar basalts are either derived directly from the lunar mantle as primary liquids (A. E. Ringwood and co-workers), or they are secondary magmas that have been differentiated by low pressure crystal fractionation acting on the primary liquids (M. J. O'Hara and co-workers). If the latter is true, the lavas cannot be used to calculate the composition of the lunar mantle with which they would have been in equilibrium at the stage of primary partial-melt formation.

Our evidence suggests a two-stage magma eruptive process. If the specimens represent solidified lava-lake material alone, the plagioclase phenocryst zoning should have continued beyond Ca67, into the groundmass. If they represent solidified surface lava, however, the plagioclases should all be alkali-depleted and of the same composition as the groundmass (Ca93). The evidence is that two environments were involved, the first permitting closed-system cooling to give zoned phenocrysts, and the second producing open-system alkali loss. Such evidence was lacking in the Apollo 11 and 12 basalts, where only "groundmass" plagioclases are involved; they are generally very calcic, although slight zoning may indicate some crystallization from thick lava flows. We propose a model to account for these Apollo 14 basalts, which also has implications for the genesis of anorthosites and of other crystal cumulates.

Mantle-derived basalt magma was poured into large, meteorite-scoured surface basins to form large-volume lava lakes. In the lake under consideration, the magma was probably a high-alumina tholeiitic basalt. Plagioclase crystallized early, probably accompanied by aluminous spinel and low-aluminous orthopyroxene. Some alkalis were probably being lost even at this stage (close to the lunar surface) to give very calcic plagioclase phenocrysts (Ca95). Loss of Na could also have inhibited olivine and Ca-rich pyroxene crystallization[13], in favour of Ca-poor pyroxene:

$$\underbrace{3NaAlSi_3O_8 + 3CaAl_2Si_2O_8}_{\text{Sodic plagioclase}} + \underset{\text{Olivine}}{5Mg_2SiO_4} + \underset{\text{Ca-rich pyroxene}}{CaMgSi_2O_6} \rightarrow$$

$$\underbrace{4CaAl_2Si_2O_8 + NaAlSi_3O_8}_{\text{Calcic plagioclase}} + \underset{\text{Ca-free pyroxene}}{11MgSiO_3} + 2Na + O$$

The calcic plagioclase phenocrysts floated to the top of the lava lake to form a thick, shielding crust. They could carry with them a lot of small, attached, magnesian orthopyroxene crystals. The density difference[12] between the plagioclase (2.7) and the liquid (3.0 to 3.2) would, in fact, permit floating of composite grains in the ratio of plagioclase : orthopyroxene (3.3) of about 1:1. This is often overlooked in explanations of magnesian minerals in anorthosites, but it is a common phenomenon in layered intrusions[10]. During this crystal-sorting process, denser minerals would settle to the floor. It is, therefore, less likely that we shall find impact disruption at this level to give many mafic cumulates on the lunar surface. Liquids could, however, be tapped with varying amounts of suspended, accumulated mafic crystals from below the plagioclase-enriched layer. As solidified lava with variolitic groundmass, similar to some of the Apollo 12 rocks (for example, 12040), they would tend to show a mafic phase on the liquidus in experimental studies. This would obscure the fact that plagioclase was a liquidus phase in the lava lake. In other words, crystal sorting in a near-cotectic liquid would yield products with diverse "liquidus" phases. It would mean that anorthosites could be derived from the same liquid as a "mare basalt", the anorthosites being enriched and the basalts depleted in europium.

At the top of the primitive lava lake, heat losses would be rapid and a temperature gradient would develop between roof and floor. Convection currents would then transfer heat from the plagioclase-rich roof zone, thus permitting adcumulus growth[10] to yield anorthosite with subsidiary magnesian mafics having little or no compositional zoning. After a thick anorthosite crust had formed, convection would diminish. The floated plagioclases would be less abundant and suspended in magma which, on cooling, would produce zoning of the plagioclase cores. At this stage, disruption of the crust by impact events probably occurred in certain lava lakes. The crust was pulverized to produce anorthosite and pyroxenic anorthosite fragments which were severely shocked and distributed widely across the lunar regolith. The underlying lava was then erupted to give thin flows of feldspar-phyric basalt of the type described here. The zoning stopped because alkali loss occurred on a large scale, and the lava precipitated calcic alkali-poor plagioclase.

If this model is applicable, we are now looking at volcanic rocks from the lunar surface that have been erupted after a period of crystal sorting. They are not in any sense primary magmas, although the bulk of anorthosite may ultimately point to a high-aluminium basalt as a dominant primary liquid. The detailed evidence provided by the Apollo 14 feldspar-phyric basalts can thus help to piece together several isolated problems, such as the genesis of anorthosites and the question of secondary magmas and of alkali volatilization. Restraints would then be imposed on models relating to the nature of the lunar mantle and the original lunar chemistry in terms of volatile elements. We do not wish to imply that there must be a direct historical connexion between the feldspar-phyric basalt—norite—anorthosite suite and the mare basalts. There is, however, a feasible connexion in terms of magmatic processes. Slight differences in primary magma composition, and differing timescales for the breaching of lava lakes and the loss of volatiles, would lead to appreciable differences in crystallization sequences and phase equilibria.

Fractionation of plagioclase in the lunar crust probably occurred at 4.6 b.y. on a much greater scale than in lava lakes. We are more concerned with the fact that the same type of primary basalt could have been present in later lava lakes, illustrating more clearly the processes associated with anorthosite–norite–feldspar-phyric basalt cogenesis. Plagioclase removal would be early, and would therefore not introduce significant Rb-Sr fractionations[14] during subsequent crystal sorting to produce the type of diversity seen in the Apollo 12 basalts. We favour crystal sorting, discussed above, for the anorthosite–norite suite, predominant as the "magic component" in the lunar regolith soils. Such a process would produce variable adcumulus effects, and hence variation in the Fe/Mg ratio of the silicates to give Type A and Type B anorthosites[12], without a compensating variation (by either zoning or reaction) in the alkali-depleted plagioclases formed near the lunar surface. Fractionation of lunar basalts gives rise to phases rich in K, REE, P and Zr. These are associated with rhyolitic glass which probably had a high viscosity in the liquid state and was immiscible with the ferrobasalt liquid[15]. This KREEP-rich liquid appears to have concentrated among the uppermost plagioclase-pyroxene, noritic cumulates (but not among the extreme adcumulus anorthosites). It is also present in isolated patches in the mare basalts and in the feldspar-phyric basalts. We consider it to be an *in situ* residual fractionate[11], but it has a high Rb/Sr ratio and may be a contaminant[14] from a rhyolitic fraction produced earlier. It would melt easily and could be the contaminant necessary to explain the variable initial $^{87}Sr/^{86}Sr$ in the mare basalts[14]. Again, the idea that a single lava lake could produce various erupted basalt lavas is still a possibility, although a multi-lake terrain would superimpose greater variety.

We would like to see europium analyses made on the Apollo 14 feldspar-phyric basalts, because the plagioclase phenocrysts ought to provide evidence for or against the hypothesis[16–18] that Eu^{2+} enters preferentially into the plagioclase structure. Age data on these rocks would also be highly significant; if they are associated with an early, crustal anorthosite generation, they ought to yield isochron ages of the order of 4.6 b.y. ; but if they yield younger, mare-basalt type ages (with old model ages) then we must either accept a metamorphic event of that age (difficult, in view of preserved feldspar zoning and residual glass) or consider closer genetic relationships between the feldspar-phyric, high alumina basalts and the low-alumina mare basalts.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Model of Early Lunar Differentiation

It has been suggested that one of the first major chemical differentiations in a planetary body such as the Earth will involve segregation of an Fe-FeS liquid[1,2]. This is because the eutectic temperature of this system (referred to here as Fe-S) is 990° C and is much lower than the temperature required to melt silicates (~1,100° C). The eutectic temperature is relatively insensitive to pressures[3] of at least 30 kbar.

The surface regions of the Moon have been melted and silicates differentiated at ~4.6 billion yr ago[4,5]. It is certain, that any Fe-S present will melt long before the silicates and because of its greater density will sink into the interior. Because of the small gravitational size of the Moon and because of the time required to accumulate any radiogenic heat, the interior of the Moon at the time of surface melting must have been cold; thus the sinking Fe-S liquid will be trapped at some depth.

Sonnett *et al.*[6] have described evidence for a layer of high electrical conductivity in the Moon at a depth of 250 km. They suggest that this is caused by compositional or phase change. It is improbable that phase changes, caused by partial melting in the silicate compositions appropriate to the Moon, can result in an electrical conductivity increase of three orders of magnitude. More probably, a major compositional change is involved. We suggest that this is an Fe-S layer (Fig. 1). In a Moon containing, as in some meteorites, about 5% by weight of FeS, melting of the outer 200 km will produce an Fe-S layer roughly 10 km thick.

If the Moon was an Earth satellite in synchronous rotation at the time[7] of melting, tidal forces and the then rapid rotation of the Moon would produce bulges in the Fe-S liquid layer both towards and away from the Earth with associated thinning at the poles. Further, differential gravitational effects between the rigid interior and the surrounding Fe-S liquid layer could introduce a basic asymmetry in the mass distribution of the Fe-S layer, the mass being greatest in the Earth-facing side (Fig. 2), analogous to models suggested by Baldwin[8] and Smith *et al.*[9]. Such a distribution of mass in the Fe-S layer is in qualitative agreement with the three unequal lunar moments of inertia[10]. Hydrodynamic instabilities of the type described by Elsasser[11] can produce downward bulges in the layer and consequent localized concentrations of Fe-S. We shall refer to these Fe-S concentrations as "fescons". We expect the fescons to be preferentially located on the near side of the Moon, reflecting the asymmetry of mass in the Fe-S layer caused by the tidal forces.

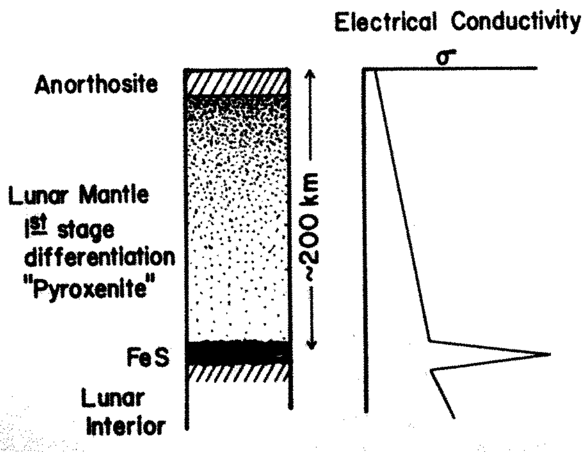

Fig. 1 Position of Fe-S layer in the Moon 4.5–4.6 × 10^9 yr ago.

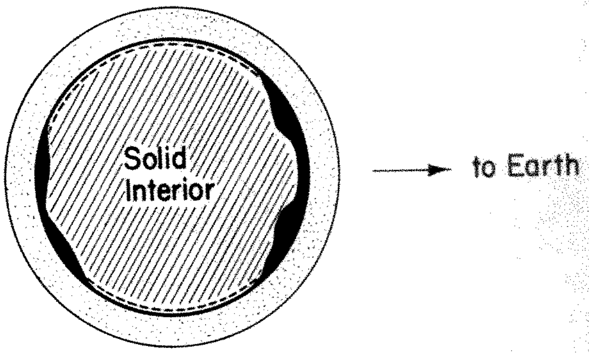

Fig. 2 "Droplets" of Fe-S form fescons at sites of tidal bulges.

The Moon's observed principal moments of inertia cannot result from a homogeneous body having the Moon's known shape. Muller and Sjogren[12] have shown that the circular maria are associated with positive gravity anomalies attributed to excess mass (mascons) under these regions. Mascons near the surface[13-15] can explain quite precisely the known ratios between the lunar moments of inertia. But their masses are a factor of ten too small to account for the magnitude of the moments of inertia[16]. In our model, variations in the thickness of the deformed Fe-S layer from 10–20 km produce fescons of sufficient mass (10^{21}–10^{22} g) to explain the observed moments of inertia.

Using the treatment of Morgan[17] and assuming a viscosity in the lunar interior of 10^{26} poises[18], a fescon of mass 10^{22} g would sink only 40 km in 4.5 billion yr, even if the mass were in the form of a uniform sphere. Because the fescons would probably be disk-shaped, the excess pressure, and hence the rate of sinking, would be appreciably less. Any minor sinking would tend to produce subsidence of the overlying material resulting in shallow circular basins.

It has been argued recently that in conditions of Fe-S segregation, the normally lithophile alkali metals, K, Rb and Cs, may exhibit chalcophilic behaviour[19,20]. In the Moon, therefore, we might expect that the segregation of Fe-S from the surface materials has impoverished them not only in chalcophile and siderophile elements, but in the alkalis as well. Heat production in the fescons by decay of ^{40}K with a half life of 1.3 billion yr would be most pronounced in the first billion years or so of lunar history, while the U and Th heat production in the outer zone of silicates would be both more uniform with

(*Continued on page 290*)

REVIEW SUPPLEMENT

Slowly but Steadily with Information

THE doctrine of the free flow of scientific information is a little like the concept of democracy—everybody is for it in theory but most people hope against their better judgment that they will not themselves be too seriously diverted from their individual objectives. At the beginning of October, UNESCO held a conference in Paris to make plans for the development of what is called a "World Science Information System". The occasion, no doubt the first of many, was organized around a careful study report prepared in the past three years by a committee of sensible men sponsored jointly by the International Council of Scientific Unions and UNESCO. Naturally enough, those who worked hard, sometimes with stars in their eyes, to make the conference a success will have been disappointed that it turns out to be less concerned with the proper organization of the exchange of information than with the question of whether the proposals put forward in Paris two months ago would give a fair crack of the whip to developing countries. The complaint seems to have been that only two of the twenty-two recommendations put forward for consideration by the conference dealt specifically with the problems and needs of developing countries. "Is this not a measure of how we are neglected?" was the cry. The simple answer, and the truth, is of course that in developing machinery for the exchange of scientific information, it is in everybody's interests that the methods now developed should serve not merely for the present and the immediate future but for the decades ahead when, with any luck, many of the developing countries will have reached and even surpassed the stage of development which pertains in societies now considered to be advanced. The developing countries are right constantly to remind their well-to-do competitors that foreign aid and technical assistance are at present being provided on too niggardly a scale, but that is quite a separate matter.

The proposals which form the bread-and-butter of the conference in Paris are known by what seems to be a code name—UNISIST. In modern language, to describe the plans now made as a "World Science Information System" is over-ambitious and even misleading. What the working group responsible for the documents discussed in Paris seems to have had in mind is that it might be possible, by timely and quick-witted intervention from an international base, to influence the development of national policies on the handling of scientific information in such a way as to bring about valuable economies, both in direct cost and in the saving of scientific effort that might otherwise be wasted on duplicated research. This is a sensible approach to a problem or set of problems for which there can of course be no ideal solution—the needs of those who use scientific information and the character of scientific information itself are changing too quickly for it to be feasible to design in advance an information exchange system that will last for the rest of time. The difficulty is, of course, that in attempting to coordinate national activities in the interests of efficiency and economy, success requires not merely an acknowledgment that coordination would be worthwhile but also a degree of flair. It remains to be seen whether UNESCO will be able to bring to this task more than the pedantic bumbledom with which it usually tackles jobs like this.

For the time being, it seems that there will be no separate budget for work under the UNISIST banner, but that it will be possible to scrape together from the existing UNESCO budget enough money to begin work on a new World List of Scientific Periodicals and to prepare for a more ambitious programme in 1973. This perhaps is just as well. No harm will be done if those concerned with the processing of scientific information have a little more time to think about the practical implications of the recommendations discussed in Paris. And the first question to be asked, not merely by the professional processers of scientific information but also by those whose activities in research laboratories give rise to scientific information, is what the function of the free exchange of scientific and technical information should be.

This is a field in which means are too easily and too frequently confused with ends. The purpose of exchanging scientific information is now what it has been for the past three centuries—to stimulate the progress of research and to provide practical assistance to those who may be able to apply the results of scientific research. In basic research, especially that of an academic character, there is no doubt that everybody profits from a full exchange of information but, at the same time, it does appear that the problems of exchanging information as such are comparatively easily mastered. The people who work in universities are, after all, usually able to keep up with what their colleagues elsewhere are doing by correspondence, by using the scientific journals, by gossiping at conferences and by using their scientific colleagues (and particularly their research students) as news hounds of a kind. In this context, however, the most difficult task in the exchange of information is not so much the provision of references to published literature, lists of titles or indexes of key words as the almost pedagogical job of helping people to understand what their colleagues elsewhere are driving at. The schemes that have been worked out in the past few years for mechanizing the scientific literature or at least the process of indexing it are naturally of great value to academic scientists, but in the last resort there is no substitute for the hard work of reading and puzzling

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out what the other fellow means. In short, UNISIST (or some other coordinating body) could help with the flow of information within the academic part of the scientific community, but its influence would not be crucial, whatever may be said (as in the UNISIST report) of the "information explosion".

Formal arrangements for the exchange of information are likely to be of greater value in applied research and development. This, certainly, is at least a part of the reason why nuclear engineering has seen the most elaborate development of information processing and exchange systems, first on a national basis under the aegis of organizations such as the United Kingdom Atomic Energy Authority and the United States Atomic Energy Commission and then internationally, within Euratom, for example, and within the International Atomic Energy Agency in Vienna. These are eminently fields in which factual information arising from research can help directly with the design of equipment, systems or research programmes elsewhere. The difficulty, of course, is that there are bound in circumstances like these to be severe limits to the altruism of those with information to give away. It is a considerable triumph that there has been as close a degree of sharing of information on nuclear energy as the International Atomic Energy Agency has been able to arrange. Obviously there is scope for a similar treatment of some other fields—tropical agriculture and medical research are obvious examples—but it is bound to be a long time before those who develop electronic components made of microcircuits, or photographic emulsions for special purposes, will be willing to see full information disseminated internationally. In other words, those who set about the design of systems for the free exchange of information must recognize that the uses to which these systems will be put will be in part at least determined by the compliance of the sources of information as well as by the demands made on the systems by the users. A more hard-headed discussion of this feature of the process would have strengthened the study report which provided the agenda for the meeting in Paris.

Within such a framework, there is a great deal of useful work that can be done. The UNISIST group quite properly makes a good deal of the work that needs to be done in standardizing the methods at present used for describing scientific information. Even on matters such as standards of bibliographic description, there is immense chaos. Although several bodies, national and international, have in the past set out to promulgate standards that would be internationally recognized, the chief result of these well-intentioned efforts so far has been not standardization but diversity. There are countless illustrations of how those first in the field of standardization have found themselves lumbered with antiquated arrangements—the 7-bit computer code developed in the United States in 1963 for ensuring some degree of compatibility between computers turns out to be less satisfactory than and incompatible with the 8-bit code now favoured by the International Organization for Standardization. And then there are fierce problems to be solved in abstracting and indexing. If UNISIST chooses to cut its teeth on problems like these, it will have a decade of hard and useful work ahead of it and long before that time is up it will have worked out an indispensable place for itself in the international scientific community.

To the extent that the specific programme outlined in Paris (and not yet financed by UNESCO) is of this nature, nobody will complain. Unfortunately, there is a tendency in the document for ambition to run ahead of what may be feasible. The report asks, for example, that there should be an attempt at this stage to enlist the cooperation of the International Telecommunications Union and similar bodies in experiments on the mechanics of transferring scientific information in printed or telegraphic form from one place to another. There are schemes for using Earth satellites in the same connexion. The UNISIST programme also asks for programmes for the evaluation of efficiency in the handling of scientific information (which is sensible and necessary) and for the evaluation of research and information science (which on the face of things would be best left to the organizations which are responsible, on a national basis, for sponsoring research). The most obvious difficulty, of course, is that if UNISIST is to spread what little funds it can command over such a wide and difficult field of inquiry, it will find that it can do nothing properly and its reputation for good sense will be lost before it can be used. In all the circumstances, there is a great deal to be said for modesty and the containment of ambition. That is another reason why no harm may be done if UNISIST has to kick its heels, for another year or so, waiting for the money to come through.

UNISIST is on still more dangerous ground in what it has to say about the development of policies on the exchange of information. To be sure, the need that some information should be kept secret because governments want it kept secret is acknowledged, but grudgingly. The UNISIST document considers that there is even less reason for confidentiality in the sharing of information which may be of economic or industrial importance—the difficulty here is not so much that free exchange is unlikely to be possible but that by pretending that free exchange is ultimately inevitable, UNISIST runs the risk of seeming unrealistic. (Exactly the same criticism can be levelled at the UNISIST declaration on copyright, which the report describes as "another form of information monopoly".) UNISIST says that "the matter has been brought up again and again as the development of new information technology raises problems of proprietorship that were not envisaged twenty years ago", when the Universal Copyright Convention was developed. It complains that the need to obtain clearance for the reproduction of documents of all kinds is a barrier to the free flow of information and asks that there should be a serious examination, by all the countries adhering to UNISIST, of the question how far it would now be practicable to abandon copyright on scientific material. This is, of course, a radical issue. In journals such as *Nature* and in books of all kinds, the author is the one who holds the copyright and, although there are many circumstances in which he does not care how freely his material may be reproduced elsewhere than in the place in which it was first published, there are also circumstances when it would seem to him to be grossly unfair that free reproduction should be assumed as a right. But especially where the publication of books is concerned, the abandonment of copyright would also frequently mean the end of a great many commercial publishers. The naivety of this recommendation is yet another reason for fearing that UNISIST will have to learn to walk before it runs as hard as its prospectus promises.

General Books

Statistical Papers

Statistical Papers of George Udny Yule. Selected by Alan Stuart and Maurice G. Kendall. Pp. viii+447. (Charles Griffin: London, August 1971.) £6.90.

George Udny Yule, who was born in 1871 and died in 1951, was certainly a peer of the statistical realm. Some knew him as one of England's gentlemen but many more as an innovator of statistical techniques and a teacher of great capability and understanding. The book by which he will be known to most (and recalled with gratitude) is the *Introduction to the Theory of Statistics*, first published in 1911 and still in substantial demand with the fourteenth edition (1950) being the fourth in collaboration with Dr M. G. Kendall, one of the selectors for the volume now under consideration. To say "review" would be impertinent as well as discourteous, therefore let it be stated that the distinguished selectors have carried out with great understanding their difficult task of exclusion: the complete bibliography shows their problem clearly.

To quote from the preface, "The reason why these twelve papers were selected . . . is that they contain work whose historical significance in the development of statistical methods is matched by its continuing importance". To the selected papers is added the account of the man written by Dr Kendall (*J. Roy. Statist. Soc.*, A, **115**, 156; 1952). The selected papers fall into three groups: theory of association and correlation, epidemiological studies and the analysis of time series.

The first group (1900, 1903, 1907 and 1912) form the basis of current practice especially with respect to the difficult problem of notation. In fact, Yule's work on measures of association between attributes is still the principal reference and it is of importance to current and future generations of students that they should know that the date is not significant in any sense of being old and out of date. The selectors note that these four papers do not exhaust Yule's work in this field and an item drawn from the bibliography "On the interpretation of correlations between indices and ratios" (*J. Roy. Statist. Soc.*, **73**, 644; 1910) is of considerable importance in economic assessment.

The second group (1910, 1915, 1917 and 1920) are in the field of epidemiology but they contain the fundamental work (jointly with the late Professor Major Greenwood) on the negative binomial distribution; a form which has very wide-ranging applications both as a logical model and as a descriptive device. Moreover the 1910 paper is an early example of what is now known as sequential analysis and the 1920 paper is an original example of mixtures of distributions upon which a great deal of more recent work has taken place.

The third group (1921, 1926, 1927 and 1945) are on the analysis of time series whereas the philosophy of serial correlation, the correlogram and the autoregressive series (as a stochastic model) is set against that of classical harmonic analysis. This step is now seen to have been vital for the understanding of economic and social activities where man's memory plays an important part.

Looking back it is interesting to see the time sequence of these three groups; interspersed in these is a range of other papers, including all Yule's work on the statistical analysis of literary style and vocabulary, which should also not be overlooked by teachers, students, research workers and practising statisticians now and in the future. The selectors and publishers are to be congratulated and commended on this volume to celebrate the centenary of Yule's birth. W. R. Buckland

Postal History

History of Letter Post Communication Between the United States and Europe, 1845-1875. By George E. Hargest. (Smithsonian Studies in History and Technology, No. 6.) Pp. ix+234. (Smithsonian Institution: Washington, 1971.) $4.25.

On reading the title of this book two questions immediately spring to mind: why 1845 and why 1875? The answer to the first is tied up with the trade and business rivalry between the United States and Great Britain. A British steamship line (Cunards) had become so efficient that their regular fourteen-day service between Boston, Massachusetts, and Liverpool (the "Atlantic Shuttle") had forced the American sailing packets well into second place. The British ships carried the mail, cabin passengers and "fine" freight; the Americans carried the coal. American pride was piqued and Congress was concerned about the security aspect of all the American mail to Europe being carried by British ships. In 1845 an act of Congress was passed subsidizing the United States mail packet ships, in an attempt to overcome British domination of the Atlantic service.

Why 1875? To answer this we have to go back to the time before the General Postal Union. Then a letter from the United States to Europe could not be fully prepaid, some of the postage had to be paid in the United States and some in Europe. When a postal convention existed, accounting between the post offices of the contracting countries was established which made it possible to pay the whole postage on a letter sent or received. On January 1, 1876, France, the last of nineteen European countries to do so, placed in force the provisions of the treaty of Berne and became an active member of the GPU.

The history of the letter post communication between the United States and Europe between the years 1845 and 1875 is told in this book. It is divided into sections describing the negotiations of the United States–Bremen, Germany, Postal Arrangement of 1847; the postal treaty with Britain (December 1848); postal relations with France, and the United States–French Postal Convention of March 1857; the Prussian Closed Mail Convention; postal relations with Belgium 1844–1868; amendments in the 1860s to the above convention and the operations of the steamship lines; postal conventions effective after January 1, 1868; postal relations with France 1870–1876; depreciated currency covers and finally the postal rates between the United States and all foreign countries.

The book is obviously the result of much painstaking research, largely drawn from primary sources. It contains many illustrations of postal covers ("the cover being to the postal historian what the artifact is to the archaeologist") and is very well indexed. It makes a worthy addition to any postal historian's bookshelf. David W. Hughes

Old Affinity

Affinity and Matter. By Trevor H. Levere. Pp. xvii+230+14 plates. (Clarendon: Oxford; Oxford University: London, September 1971.) £4.50.

Levere opens this book with an excellent chapter summarizing the major eighteenth century views on affinity. Then follow the four principal chapters chiefly concerned with setting out the speculative views of Humphry Davy, Michael Faraday, Jöns Jakob Berzelius and Hans Christian Oersted. The final two chapters respectively describe the input from the rapidly growing field of organic chemistry, and the mid-century anticipations of what became thermodynamics. The first chapter and the last two thus provide a historical setting for the author's major concern to dissect the intricacies of early nineteenth century metaphysical speculation on affinity.

Levere sees "chemical affinity as a unitary concept in nineteenth century chemical theory" (page vii), but as the material is presented, it seems more a projection of his own fascination with the speculative than a believable historical reality. He devotes more pages to the Kantian metaphysics of the poet Samuel Taylor Coleridge than to the two contemporary books on chemical affinity by Claude Louis Berthollet; he treats Boscovich's point-atomism in more detail and with more sympathy than the operational atomism of John Dalton. Though such an emphasis is consonant with the author's expressed desire to move history of chemistry away from a concern with only those events that led directly to the "truths" of present day chemistry, Levere's interpretation seems as distorted as the "Whiggish" one he is trying to replace.

Nonetheless this is an impressive book, both for what it contains and the scholarship that produced it. The empirical basis for most of the speculations about the nature of chemical forces was Davy's announcement in 1806 that electrical attraction and chemical affinity might be the same thing. Davy's own undisciplined speculations get the fullest treatment, but Levere gathers his evidence from many scientists and much of it from manuscript sources. The sheer quantity of speculation from men known chiefly for their experimental discoveries is significant and tends to confirm the sense of uncertainty visible from other evidence at this time, a disquietude that chemistry's progress appeared to be accidental and its basis unphilosophical.

The material in this book has been previously little attended to, probably because such speculations have not been thought to have contributed to the progress of chemistry. Levere, however, seems to believe that their metaphysical views led these men to their scientific discoveries. For example, he states that Oersted's metaphysical outlook "was eminently successful in furnishing him with theories that led to discoveries, and as such it deserves attention" (page 139). This is an enormously important claim, but Levere hardly attempts to prove it. He does not describe the particular hypothesis that Oersted had in mind when he discovered the relationship between electricity and magnetism; he does not show how that hypothesis could have been derived from Oersted's metaphysics; he does not describe the experiment nor the relationship it demonstrated. Nonetheless, Levere has shown that these scientists cared very deeply about their speculations, and future biographers will probably find individualized explanations for the relation of metaphysics to discovery.

The material in this book is important and largely new. Whether or not he agrees with the interpretations through which it is here presented, no historian of nineteenth century science should neglect it.

ROBERT SIEGFRIED

Medical Care

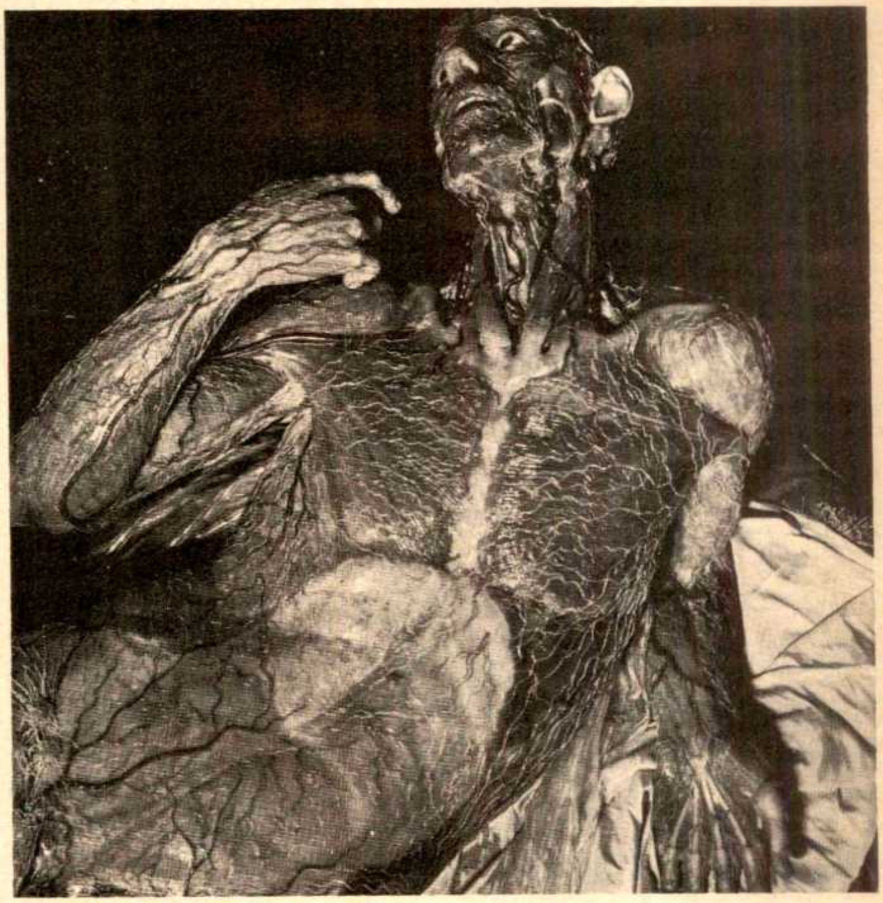
Medical History and Medical Care: A Symposium of Perspectives. (Arranged by the Nuffield Provincial Hospitals Trust and the Josiah Macy jun. Foundation.) By Gordon McLachlan and Thomas McKeown. Pp. xii+244. (Oxford University: London and New York, 1971.) £3.

THIS book is the record of a symposium held in London in October 1970 under the auspices of the Nuffield Provincial Hospitals Trust and the Josiah Macy jun. Foundation. The purpose was to explore and evaluate the history of the human experience of disease in an attempt to ascertain how far such historical studies are capable of contributing to the solution of contemporary problems.

In the preface Lord Cohen of Birkenhead comments that it is far too early to assess the ultimate value of the symposium. "Perhaps as much was gained in the informal meetings with one's colleagues as in the more formal sessions, and perhaps future meetings of similar type will help to illuminate the persisting shadows."

The book is, in effect, a series of essays, each of which is followed by a summary of the original discussion on it. They comprise two papers by Thomas McKeown, on a sociological approach to the history of medicine and a historical appraisal of the medical task; changes in the supply and characteristics of American doctors in the twentieth century by John Z. Bowers; historical trends and future prospects in public health by George Rosen; evolution of medical practice by John Brotherston; historical discontinuity, hospitals and health services by Paul J. Sanazaro; the influence of medical technology on medical services by Bernard Towers; on measuring economic benefits of health programmes by Rashi Fein, and a contemporary view

Science in Florence



One of a collection of anatomical models made in wax by Clemente Susini (1754–1814) which can be seen in the Specola Museum, Florence. This city has a history of scientific achievement dating from Etruscan times which is recorded and profusely illustrated in *La Scienza a Firenze* (edited by G. Chiarelli for the Florence Tourist Board. Pp. 205. Edizioni d'Arte Il Fiorino, Florence, 1971).

of the historical influences on medicine by Henry Miller. References are appended to each discussion.

Dr Gordon McLachlan completes the postscript by saying that the symposium may prove to be the modest beginning of a movement towards a better understanding of problems common to all countries. It is by this standard that the book should be judged.

There were fourteen British and ten American participants in the seminar, most of whom were medically qualified, and the book, not unnaturally, reflects this pattern, for it discusses Anglo-American medical history and medical care. As the theme develops, from the evolution of medical practice to the measurement of economic benefits of health programmes, those with field experience in "developing" countries may find the gulf between the problems and resources there and those of the wealthy and sophisticated societies under scrutiny almost terrifying. It is going to be difficult to find common ground for future discussions, for the solutions must also be different.

The quality of the essays is uniformly high and the reader is not unduly distracted by the transition from English to American styles of writing. Some are controversial, notably those by McKeown. Others are monographs, complete in themselves, and Brotherston's essay on the general practitioner is an outstanding example of this. So also is Rashi Fein's contribution on the measurement of economic benefits of health services.

The purpose of the final essay by Henry Miller was to review those that preceded it and to seek pointers to forward planning. It is an amusing and at times devastating commentary on the proceedings which should be read in full, but it can be epitomized by his verdict that: "If anything is clear from this meeting it is that we cannot predict medical developments during the next fifteen years. How can we in all conscience return to our hospitals and put forward plans that claim to meet the needs of fifty years ahead?"

In short, this book is an authoritative record of the current anxieties and problems in the field of medical care in Britain and the United States of America. A. LESLIE BANKS

Bioethics

Bioethics: Bridge to the Future. By Van Rensselaer Potter. Pp. xvii+205. (Prentice-Hall: Englewood Cliffs, New Jersey. March 1971.) $5.95 cloth, $3.95 paper.

THERE is a need, apparently felt by a number of individuals who have had a long and productive research career, to gather together in one place their thoughts on a variety of disparate topics. It is an easy way to build a book out of past material, labour saving and doubtless ego-gratifying for the author; presumably profitable for the publisher. If it is dressed up with a new and trendy title, the unwary will believe that the book is really a book and not a sort of *paella* made with the left-overs. There is of course nothing against reissuing one's minor or even seminal thoughts in this way; one recent book containing the collected views of a respected Chinese scientist-cum-political leader has reputedly sold into the millions. But I do feel that publishers should warn prospective purchasers that they should not buy on the assumption that here is a ne wbook.

Disregarding, then, the pretentious title, what is one to make of this *pot-pourri*? Dr Potter is evidently a likeable, moral and concerned man; his thoughts radiate the common sense of the American liberal, convinced that "we need to compete with the communists in the field of ideas and not merely in the production of corn, hogs and missiles". His contribution to the competition is, on the one hand, a straight down-the-line defence of objectivity and scientific progress, conducted, however, without the clarity of Jacques Monod's *Le Hasard et la Nécessité*, and, on the other hand, an uneasy but undefined feeling that not all is well with the concepts. To bolster them comes "bioethics", a *mélange* of Teilhard de Chardin and ecological concern. If Dr Potter does not go all the way with those *Nature* has in the past described as the "econuts", and he is far too sound a man to thicken the air with doomful prognostications, he does believe in biological responsibility. . . . "An urgent task for bioethics is to seek biological agreement at the international level."

This is all very well intentioned but rather far from the real problems of contemporary society, which are not so much the accidental as the deliberate consequences of the application of science and technology. Thalidomide, happiness and Pandora's box all get references in the index. The Garden of Eden and the ethical revolution are there, but Vietnam and the military-industrial complex do not appear; the problems of the third world countries are encapsulated in the limpid but scarcely acceptable conclusion that ". . . the United States, Western Europe and Russia are the materialistic giants while India is a country with essentially the religious attitude towards progress". One fears that Dr Potter's irony was at best unintentional.

There are some good things in the book, though unexpected simply insofar as it is difficult to predict anything about its contents; two interesting chapters on an optimum environment for man, which draw on the author's own research; a parenthetical sideswipe at Jansenism; and a brave and intriguing first chapter. This chapter, although entitled misleadingly "Bioethics", is an attempt by Dr Potter, under the heavy and acknowledged influence of T. S. Kuhn's views on paradigms in science, to extract what he believes to be the twelve central paradigms of contemporary mechanistic biology, ranging, in hierarchical order, from those concerning molecular systems, to those of physiological adaptation. Whatever the merits of the Kuhnian analysis, this particular exercise is worthwhile, and could well be built in conceptually to the training of biologists, who need to be taught more clearly the epistemology of their subject as well as its "facts".

STEVEN P. R. ROSE

Nonscience

Nonscience . . . or How not to Rule the World. By Brian J. Ford. Pp. 206. (Wolfe: London, September 1971.) £2.00.

SOME of the elements of which *Nonscience,* by Brian J. Ford, is composed made me laugh aloud; others exasperated me to about the same degree. Its publishers promise us a satirical look at our age, and Mr Ford makes his intentions clear immediately. This is an age when "accepted codes of technological betterment may replace our notions of humanity"; but there is no sense in wanting to abolish technology, nor virtue in being anti-science. The enemy to be driven out is "pragmatic, self-fulfilling, narcissistic Nonscience", which Mr Ford defines in terms of its mechanics, its effects, its language—the stock-in-trade of a new breed of individual, "the expert".

The essential feature of the expert is absolute dedication to data (rather than to new ideas and imagination) which he uses omnisciently to substantiate whatever case happens at the time to promote his own standing, usually by its getting him into the public eye. The sarcasm may be pretty heavy, but Mr Ford has a point. What exasperated me was the stance he takes for establishing it in the first place—too chip on the shouldery; too studentish, as exemplified by students who get into the public eye by posturing as self-appointed members of a depressed class. One of Mr Ford's early swipes is at the people who do technical jobs in the Department of Trade and Industry. It matters less that he's wasting his energy than that he's showing an absence of grasp on how the world works. This will make his swipes seem the less to be worried about by the people who actually work the world, when he comes, as he should, to swiping at them.

However, Mr Ford is witty and enjoys playing with words. I liked, for example, his transformation of "integrity" into "considered circumspection". He makes his own contribution to the language of Nonscience (which only the expert can understand, of course): for being concerned with what gets you into the public eye he coins the word "fashionism" — in true Nonscience language, "quasi-notional fashionistic normativity". (No prize for recognizing the true language of the social sciences!)

The body of the book consists of chapters along the way, for the expert, from training to fame. They tick off some highly recognizable ploys for scoring in examinations, for getting a PhD thesis accepted, for writing an eye-catching first paper and so on. Nonsciencemanship or sciencemanship, depending on which way you look at it. There is a historical section, which to me seemed rather strained, where he demonstrates that discoveries and inventions made by men whose names every schoolboy knows were made earlier by other men whose "quasi-notional fashionistic normativity factor" (quFN Factor) was just too low. Coming to some of the experts *de nos jours*, he has very tasty things to say about, for example, Professor Christiaan Barnard and Dr Desmond Morris. (The piece on "transplant fashionism" is deliciously well researched.)

The book ends in a hail of miscellaneous swipes, some of them about as significant as shying at coconuts, others —for example, on current sex education —based on thoroughly sound human feeling. After that there's an examination paper which tests the reader's capacity for making the grade as an expert. To sum the book up: for my money there's too much of it, too many shallows between the occasional deeps. That's on the one hand. On the other, it would be ungracious of me not to say it made me laugh and Mr Ford's point is worth taking. And if he is lucky, he may plant his word "fashionistic" in current speech. WILLIAM COOPER

Arms Control

Impact of New Technologies on the Arms Race. Edited by B. T. Feld, T. Greenwood, G. W. Rathjens and S. Weinberg. (A Pugwash Monograph.) Pp. xvi+379. (MIT: Cambridge, Massachusetts, and London, April 1971.) $12.50; £5.85.

MOST conference reports make for rather loose-jointed books and this one, a symposium on technical aspects of the arms race, is no exception. However, the tenth in a series of International Pugwash Symposia, held at Racine, Wisconsin, in mid-1970, features some chapters of very direct bearing on control of the arms race. Two chapters in particular merit attention—the first on ballistic missile guidance, and the second on the restriction of research and development. These two issues are of paramount importance in the control of modern armaments and illustrate the grave difficulties which seem to insinuate the Strategic Arms Limitation Talks (SALT).

D. G. Hoag, director of MIT's Apollo Guidance and Navigation Program, has given a very authoritative 105 page exposition of missile guidance technology. The significance of this ICBM development is lucidly stated as follows:

> "The development of high accuracy in ballistic missiles may be interpreted as an intent to achieve a first-strike capability by which an aggressor, by firing first, can destroy his adversary's weapons and ability to respond in retaliation. The development of high accuracy coupled with a multiple-warhead capability may appear even more sinister."

The US development and deployment of MIRV-missiles (multiple, independently targetable, re-entry vehicles) thoroughly confuses the arms race, raising both quantitative and qualitative problems for arms control. How many warheads (MIRVs) are aboard each missile? What is the quality of the missile guidance system?

Any dependable answer to the first question must inevitably boil down to on-site and, in fact, in-silo inspection. It is complicated by the fact that the Soviets have yet to deploy any MIRVed SS-9s (their heavyweight inter-continental ballistic missile); thus the inspection problem is asymmetric.

As for the question of warhead accuracy, the answer is filled with dilemmas as illustrated by Hoag's observation: "More accurate systems are almost certainly coming, and when they do come we may not know for sure that they have arrived". One could go a step further and assert that, since quality cannot be inspected, an enemy is driven to the worst assumptions. Fear of a first strike overdrives the arms race and the inability to delimit quality of a strike system sorely taxes the ability of those who would reach agreements on strategic armaments.

Arms controllers are always nervous about what may pop out of the research and development oven. Any agreements they may promote may be sabotaged by weapons zealots, who prematurely disclose advances which may take place. Jan Prawitz of Sweden's National Research Institute of Defence contributes an incisive commentary on restricting research and development in which he concludes:

> "There is, therefore, no general way of controlling military R and D, as this control would sometimes have to deal with the intentions and thoughts of individual scientists. In specific areas, however, practical measures might be envisaged."

He suggests one—the nuclear test ban (where, alas, the treaty has not slowed the clock of weapons technology) and another—a MIRV test ban. The latter is no longer feasible because of the asymmetry in Soviet and US testing and it seems that MIRV is a runaway technology which will elude the grasp of the Strategic Arms Limitation Talks.

The United States appears to be racing itself, not competing with the Soviet Union, as it seeks to exploit military technological opportunities.

RALPH E. LAPP

Abstracts

Abstracts and Abstracting Services. By Robert Collison. Pp. 122. (Clio: Santa Barbara, California, and Oxford, May 1971.) $4.75.

THIS book gives a fairly wide survey of the history and current practice of abstracting, and deals with the nature and style of abstracts, the writing, editing and indexing of abstracts, as observed in practice, and to a lesser extent their publication. There is a special chapter on the early history of reviews and abstracts; present services are also rapidly scanned, and there is an appendix of some five hundred titles; there is also a useful reading list of papers on the subject. There is a two-page chapter on the possibilities of mechanizing abstracting. The index covers mainly authors and institutions, but otherwise not more detail than section headings.

The writing is straightforward and clear, although in parts of the book the descriptions are far too much like a catalogue, instead of an informed discussion. The examples, and hence the rather limited discussions, are largely taken from the humanities and social sciences, with relatively few references to scientific and technical journals (though the appendix lists more). Considering that the big developments in modern abstracting, the major demand, and the outstanding examples of abstracting services have been in the scientific and technical fields, the imbalance of the book's approach becomes increasingly obvious. *Chemical Abstracts* is given three or four minor mentions (chiefly in the "early history"), and its innovations in production and outstanding indexes, as well as the tape versions, are not described at all. POST is listed, but not CBAC. *Bulletin Signalétique* is mentioned, but not the

Referativny Zhurnal. Subject indexing is given scant attention, although it is the essential tool for retrospective searching, especially since computerized indexing, mentioned several times, is not yet at all efficient.

The book is in no way a textbook and those wishing to learn how to abstract and produce an abstracts journal will have to look elsewhere. As Mr Collison's intention is, however, to provide an analytical survey of the subject, this is not a fault, but he does include some advice in places in the first half of the book, and then betrays at once his lack of any authoritative knowledge of the techniques of the subject. Abstracting is not really in the field of librarianship. Thus, on page 3, Mr Collison defines an abstract as "the terse presentation, in (as far as possible) the author's own language, of all the points made, in the same order as in the original piece of primary document information". In my opinion (after years of teaching abstracting) this is dangerously misleading. In most, if not all, subjects it is important to aim for some consistency in abstracting style, and of course to standardize terminology (for example, of units, chemical compounds), especially to help subsequent indexing, and it is also always desirable to present the information in a simple logical order (correctly given on page 27) so that communication with the reader is clearly established, whereas many papers and authors' styles are far from this ideal order.

In discussing the vexed question as to who should abstract, the existence of the trained abstracter is ignored. Advice on the writing of abstracts includes apparent approval, in some cases, of a telegraphic style not acceptable in good journals. There is a suggestion that a slanted abstract, considered somehow as different from a discipline-oriented or a mission-oriented abstract (and this latest American jargon is not helpful), emphasizes only a subject-oriented portion of a document; this, again, is misleading: a slanted abstract is desirable in any special subject field, and although it should emphasize those subject interests it should still give an adequate, though brief, statement of other parts of the paper. The advice on abstracting technique — reading the paper two or three times, underlining or making marginal notes of important passages (and thus ruining the journal), and then "constructing a narrative"—will obliterate the desired logical order of information and tend to make the abstracter copy the author's style and language. Consider the effect when abstracting a German paper! The better technique is first to skim the articles, bearing in mind the desired logical order (purpose, methods, results, conclusions, side issues) and identifying those points; the whole paper can then be read somewhat selectively, to note more efficiently the necessary detail; the actual writing is thus greatly eased.

As regards the citation of the title, authors and journal references, examples of different practices are quoted, but there is no suggestion of a suitable standard. Incidentally, the problems of abstracting patents are entirely overlooked. There is also a strange suggestion that an abstract should never include a negative statement (though such a statement may be as important as a positive result) because a computer could not then deal correctly with keyword selection from a taped record. So much the worse for computerized indexes! Many other minor matters might be raised, but these examples are perhaps sufficient for my purpose. The criticisms are indeed made more in sorrow than in anger. A more or less historical survey is interesting; it is an accurate treatment of the many and varied current problems which is urgent. It must be based on wide experience.

J. FARRADANE

Physical Sciences

Relativity and Reality

Theory of Relativity Based on Physical Reality. By L. Jánossy. Pp. 317. (Akadémiai Kiadó: Budapest, 1971.) £5.

The Conceptual Foundations of Contemporary Relativity Theory. By John Cowperth Graves. Pp. xi+361. (MIT: Cambridge, Massachusetts, and London, May 1971.) £7.

REVIEWERS perform an important function and should not be irritated. Jánossy's book has no index (a serious omission). Graves's book has a vile purple jacket, with white printing on it (hard to read); the headings of the pages are put at the foot (a silly gimmick); the notes (which should be footnotes) are collected at the end, and how this made me curse! For example, I am thrilled to read on page 53 that Wheeler gives me credit for introducing the notion of a "plan". What plan? Ha, there is a note 17. But where? Feverishly I turn to the back of the book. Frustration! I must know the chapter. Back to page 53, but it does not say what chapter. Leafing back, I find its number. Now once again to the back, and the required information is mine. But, to be frank, I am by that time frustrated and angry at this foolery. So two pieces of advice to publishers: (*a*) if a scientific book is worth printing, it is worth indexing, and (*b*) the place for headings is at the head and the place for notes at the foot of the page. I have got so cross over all this that I must cool off for a moment before proceeding with my responsible task.

These two books are about relativity, but there the resemblance ends. Jánossy's style is simple, concise and direct, as fits a man interested in "physical reality". Graves floods the page with philosophical polysyllables, and one gets the impression (perhaps wrong) that what he has to say could be said much more briefly. Jánossy's approach to relativity is very individualistic ; he insists on his specially devised notation and terminology, but in the end one finds him safe on the mountain-top, refreshing himself with old wine in new bottles, labelled (spuriously, I think) "physical reality". Graves, in the manner of philosophers, is not really interested in getting anywhere and floats around the mountain in a helicopter, looking at the view from many aspects, the accompanying music being supplied by a host of other philosophers ("As A. has remarked . . ." or "As B. has pointed out . . ."). At the end, having thoroughly inspected the Einsteinian peak, the helicopter proceeds towards Wheeler's geometrodynamics, an object which is to be described as rock or cloud according to the personal assessment of the observer.

But, to quit metaphors (as if one ever could), Jánossy tells how he got acquainted with relativity at a comparatively early age; he had some difficulty with some of Einstein's concepts, but, being young and enthusiastic, he convinced himself in the end that he could understand those concepts; in trying to explain the theory to others, he learned the "language of relativity" and gradually "got used to" the theory. But a certain "bad feeling" remained; in the end he became convinced that from the philosophical point of view the concepts had to be changed; since about 1950 he struggled with the problem of reformulating the theory; this book represents the result of his deliberations.

Very fairly and honestly stated. Who of those who now call themselves "relativists" did not have to struggle hard with relativistic concepts? I, too, had that "bad feeling", and it was around 1950 that I, too, tried to sort things out. By adding a little here and a little there to what I learned from books and discussions, I have arrived at a reasonably comfortable state in the sense that, when confronted with any relativistic problem, I know how to begin to think about it, even though (most probably) I cannot solve it. It is an additional (and important) comfort that, although my concepts may be influenced by personal quirks, they are not essentially different from those in the minds of most relativists. Communication is possible, if difficult at times.

Jánossy frightens me. All the old ghosts that I have so laboriously driven out haunt his pages. To him, it appears, such concepts as distance, time, velocity, rigid body (experiencing FitzGerald–Lorentz contraction) and worst of all the ether—are basic and acceptable concepts. Yet, with these intolerable aids, there he sits on the mountaintop. I can view his climb only through a glass darkly, for it is veiled by unusual symbols and words (the metric tensor becomes the propagation matrix, an event becomes a four-point). The question is this: Can anyone but Jánossy understand Jánossy? If a forest of affirmative hands shoots up, I shall blush with shame at my ineptitude. If none, then at least he has had his catharsis and has satisfied himself.

Cutting through the philosophical jabberwockery, I feel at one in essentials with Graves, so much so that I can pick on trifles (or are they?) to query or criticize. Thus (page 314): "The field equations are nonlinear, a situation unprecedented in either classical or quantum physics". Nonsense: Euler's hydrodynamical equations are nonlinear. Next (page 194): ". . . the speed of light is not constant if there are gravitational fields". A meaningless statement unless the word speed is meaningful—presumably it means distance divided by time. Yes, but what is distance? Schoolboys may lay "rigid" measuring rods end to end, but in fact (real, practical fact) an accurate measurement of distance is a measurement of time. Nature offers us, not two basic instruments of measurement (rods and clocks), but only one (the clock—atomic clock, if you like). The excellent index in Graves's book has about half a column devoted to geometry, but its excellence is marred by the omission of chronometry, which is what relativity is all about. Once this is realized, the whole subject is flooded with light (in more senses than one), but Graves gives the matter only a passing reference (page 160), as one might refer to one of the inventions of the White Knight. Perhaps it would be clearer, ontologically, epistemologically, jabberwockologically, if I said it three times: There are no measuring rods. There are no measuring rods! There are no measuring rods!!

My thousand words are running out, and I shall not be able to comment (with approval) on the long discussion about the two sides of Einstein's field equations, nor (with disapproval) about the geodesic principle for test-particles, nor to express mild wonder at the view that there has been great progress in relativity since 1955 (it really depends what you mean by progress). What I shall always remember about Graves's book is that it set me to re-reading, after many years, Laurence Sterne's *Tristram Shandy* (how this came about is too devious to describe). For gravity has a second meaning ("*A mysterious carriage of the body to cover the defects of the mind*;—which definition of gravity, *Yorick*, with great imprudence, would say, deserved to be wrote in letters of gold"), and it seems to me that God can afford to laugh, Newton and Einstein to titter occasionally, but the mere acolyte is afraid to smile for fear of spilling a drop of the sacred oil.

J. L. SYNGE

Papal Galaxies

Nuclei of Galaxies. Edited by D. J. K. O'Connell. Pp. xi + 795. (North Holland: Amsterdam; Elsevier: New York, 1971.) Hfl. 134.00; $40.00.

FROM time to time in the history of any science, there arise so many paradoxes, discrepancies, and unexplained phenomena that the deepest foundations of that science are challenged. This is happening in extragalactic astronomy. Regions of space only a few light years across are found to radiate much more radio, infrared, optical, and X-ray energy than our entire galaxy (the diameter of which is about 100,000 light years). This luminosity often fluctuates considerably over periods of several years or, in some cases, during one day. Galaxies exist which are apparently connected by a bridge of luminous matter, yet their redshifts would imply velocities which differ by more than 8,000 km s^{-1}. There is increasing evidence that groups of galaxies fly apart with positive total energy. How could they have formed?

The most likely candidates for sources of these strange phenomena are the nuclei of galaxies. In our own galaxy, this central core may contain more than 10^7 stars pc^{-3}; it is not particularly active and other galaxies may have denser nuclei. Often these contain gas clouds in violent motion, emitting abnormal amounts of ultraviolet light. Some of these nuclei are observed to eject at least 10^{-6} $M_\odot$ of gas and stars, others may eject coherent objects which become radio emitters or even new galaxies and quasars. In fact, there are substantial similarities between the properties of active galactic nuclei and those of quasars. Many new observations in the last few years have made the time ripe for an extended study of galactic nuclei.

This book records the third international astronomical "study week" held by the Pontifical Academy of Sciences in the Vatican. Like its predecessors on stellar populations and interplanetary cosmic rays in 1957 and 1962, this will be a major, influential and lasting contribution. As befits its subject, the book itself is unusually massive. The soft-cover edition, printed by the Vatican, weighs $4\frac{5}{8}$ pounds. The hard-cover copy, lacking the history of the Pontifical Academy and the Papal address, printed on somewhat cheaper paper with a slightly unstable binding by North Holland, is the less massive version.

There are thirty-one papers organized into five main sections. First, an introduction by V. A. Ambartsumian summarizes the types of activity in nuclei. A striking form of this activity is jets having small bright blue condensations similar to the nucleus from which they seem to emerge.

The second main section contains fifteen papers on observations and their interpretation. Most of these are excellent reviews, with many new results, on the following specific topics: the optical morphology of Seyfert galaxies (Morgan *et al.*), the stellar content and evolution of galaxy nuclei (Spinrad), the optical spectra of galaxies and QSOs (Sargent, also E. M. Burbidge), physical conditions in the nuclei of galaxies and QSOs deduced from line spectra (Osterbrock), absorption redshifts in QSOs (McCrea), infrared emission of galaxies (Low), compact radio sources in nuclei of galaxies (Kellerman), expansion models of eruptions in quasars and radio galaxies (van der Laan), optical properties of nuclei (Sandage), comparison between the properties of the nucleus of our galaxy and that of M31 (Oort), velocity dispersions and discrepant redshifts in groups of galaxies (E. M. Burbidge and Sargent), space distribution and luminosity functions of QSOs (Schmidt), space densities and time scales for Seyfert galaxies, radio galaxies, and QSOs (Schmidt), and quasar statistics for Lemaître cosmologies (Salpeter).

The third section, on theory, contains discussions of the non-thermal emission and ejection of matter (G. R. Burbidge), the dynamical evolution of dense spherical star systems (Spitzer), massive rotators and spinars (Woltjer, also Morrison and Cavaliere), rotation and pulsation periods for pulsar models of quasars (Fowler), formation and evolution of black holes which accrete gas (Lynden-Bell), mechanisms for jets

(Wheeler), and a new theory of relativistic compact objects (Hoyle).

Observational cosmology and galaxy evolution are discussed in the fourth section which reviews the age of galaxies and globular clusters with a view to finding the Hubble constant and deceleration parameter (Sandage), the evolution of radio sources (Rees), the curious mystery of log N−log S (Hoyle), the X-ray background radiation (Friedman), and the X-ray and microwave background (Morrison).

The final section contains excellent summaries of the observational (E. M. Burbidge) and theoretical (L. Woltjer) positions, a list of observational and theoretical conclusions and useful suggestions for future work, and name and subject indices. The total ratio of observation to theory is about 3 to 1. There is also a reasonable amount of recorded discussion (about one-fifth of the book) of the papers. The quality of editing is high, although there are rare slips as when a discussion refers to previous comments or diagrams which are not recorded.

The lists of agreed conclusions resemble some of the diplomatic communiqués which emerge after heads of state meet in the countryside. The general style of the observational conclusion has the form: There is strong (increasing, extensive) evidence that . . . On the other hand, the theoretical conclusions leave the impression . . . It might be possible that . . . Most of the theoretical conclusions are really questions, and this indicates the present uncertainty surrounding the foundations of the subject.

Indeed, in his summary, Woltjer remarks: "Even though no strong controversy has developed at this conference it is very clear that, if we try to write down a set of definite conclusions from the theoretical point of view, many of our old disagreements will come to the surface very quickly. This meeting has been extremely successful in part because some of our differences have been set aside for the moment. . . ." The more conventional side of this controversy believes that the nuclei have formed by contracting from a more diffuse state and that the observations can be explained by conventional physics and standard general relativity. The alternative view is that the nuclei preceded and produced their less dense surroundings, and new laws of physics are required.

At present, it is much a matter of personal judgment whether one believes conventional physics can explain these discoveries. Do we need new laws of the redshift, new methods of releasing vast amounts of energy? Or are we just too unimaginative in applying existing theory? These questions are so difficult because the observations only supply very limited information about dozens of interacting physical processes. After observing extragalactic phenomena for many decades, it is amazing that we know so little. Yet it is even more amazing that we know so much.

WILLIAM C. SASLAW

Background to Plasmas

Sources of Plasma Physics. Vol. 1. By H. S. Green and R. B. Leipnik. Pp. 630. (Wolters-Noordhoff: Groningen, 1970.) 118 Dfl.; £3.75; $35.

THE primary object of this work, according to the authors, is to bring together in a single volume discussions of the mathematical foundations of statistical mechanics, the principles of electromagnetism, fluid dynamics and the kinetic theory of gases in order that a second (future) volume on plasma physics may be properly understood. Even in a book of this size, such an ambitious project must of necessity leave out substantial aspects of each of these subjects, particularly when more than a quarter of the available space is devoted to such diverse "mathematical method" topics as measure and probability theory, vector spaces, Fourier analysis, vector analysis, differential equations, calculus of variations and thermodynamics. Most university undergraduates and research workers have occasion to study these topics in depth before approaching the more formidable fields of magnetohydrodynamics and plasma dynamics. It is very difficult, if not impossible, to give a comprehensive account of all the relevant techniques of mathematical physics in one book. Certainly an extensive knowledge of pure mathematics is required before the relevance of the highly condensed appendices at the end of this book can be appreciated.

Before studying plasmas, almost all students will have attended substantial courses on electromagnetism and relativity, quantum mechanics, hydrodynamics and fluid mechanics. Furthermore, in Europe, such courses will have been given using SI units, whereas this book is written in CGS units and as such will have little appeal to non-mathematicians. After a prolonged struggle to master the SI system, I have no nostalgic longing for Gaussian or other discarded units and I find this return to the past, presumably intended for the benefit of American readers, annoying and confusing, particularly because the book is aimed at students of physics and engineering.

Many of the more difficult problems, for example those on drift analysis, and the publications of Russian authors receive little prominence but perhaps this will be resolved in later volumes. In a work of this kind a fairly detailed historical account is always of value. In this field there is much to be learnt from the lessons and mistakes of the past. For example, has any research worker in magnetohydrodynamics failed to rediscover Ferraro's law of isorotation? Here the historical aspect is played down somewhat and is replaced by concise discussions of the fundamental physical aspects and formulation of the associated mathematical problems.

This emphasis on physics, however, does not permeate throughout the whole book. The mathematical treatment of many problems is very sound but physical interpretations of mathematical results are very brief or non-existent.

It will be interesting to see how a prospective research student, in his first year after graduation, copes with this volume. It is always difficult to assess parts of a multivolume work in isolation, and so after the appearance of the second volume, which deals with a theoretical formulation of plasma physics, it will be possible to give a more precise estimate of this book.

C. PLUMPTON

Molecular Spectra

The Spectra and Structures of Simple Free Radicals: an Introduction to Molecular Spectroscopy. By Gerhard Herzberg. (The George Fisher–Baker Non-Resident Lectureship in Chemistry at Cornell University.) Pp. xi+226. (Cornell: Ithaca and London, 1971.) £5.25.

IN the preface to this book the author states that for forty years he had wanted to write a small book of some 200 pages dealing with molecular spectra and structure. However, as all spectroscopists know, during this period he did write a magnificent three-volume monograph of 2,000 pages. Now, at last, he has fulfilled his early ambition, and provided us with a short account of molecular spectra and structure. The role of free radicals is shown by the fact that wherever possible he has chosen the spectra of radicals rather than of stable molecules to illustrate his argument. The result is that we have an effectively complete account of the spectra of free radicals.

This is as it should be. For no one has contributed more than Herzberg to the understanding of these systems; and in many situations, on account of their very short lifetime which prevents any normal study by conventional chemical methods, this is the only way of studying their geometrical structure. How very right it is that his influence in this field should now have been recognized by the award of a Nobel Prize.

It is a strange story that we read. Thus the first chemical detection of polyatomic free radicals, for example

$CH_3 \cdot C_2H_5$, goes back to Paneth in 1929, but it took another thirty years before their ultraviolet spectra could be unambiguously obtained. Yet the study of radicals such as OH, C_3 and SiC_2 is of first-rate importance for the understanding of stellar atmospheres, and the spectra of comets are almost wholly free-radical in character.

All this, and a good deal else, is set out in this little book. There are chapters on diatomic radicals, linear polyatomic ones, non-linear polyatomics and a discussion of dissociation and predissociation. Throughout, the argument is illustrated by a superb collection of experimental spectrograms. As one would expect from someone with the experience of the author, there is a complete control of the material; the account is crystal clear, and there is an admirable index.

It almost seems ungracious to cavil about any omission; but the complete neglect of any account of electron spin resonance does leave a gap in the story. For although electronic and rotation–vibration spectra can be made to give us information about the size and shape of a radical, ESR can tell us about the charge distribution. The two types of experiment supplement each other (though, where a full resolution is possible, Carrington has shown that almost all the information that we can want about a gaseous radical can in principle be obtained from its ESR spectrum).

The Fisher-Baker lecture series at Cornell has provided some very fine volumes. The present set is in good company, and it deserves its place.

C. A. COULSON

Chemical Plant

Chemical Plant Simulation: an Introduction to Computer-Aided Steady-state Process Analysis. By C. M. Crowe, A. E. Hamielec, T. W. Hoffman, A. I. Johnson, D. R. Woods and P. T. Shannon. Pp. xiv+368. (Prentice-Hall: Englewood Cliffs, New Jersey, July 1971.) $15.59.

THE evaluation of process plant usually involves complicated and extensive procedures containing lengthy, repetitive and tedious calculations. The advent of easily accessible digital computers was therefore a boon to chemical engineers who rapidly adopted them for process design, and later for simulation of the behaviour of plants in operation. Indeed effective simulation of plant is not feasible without the use of a digital computer. The useful result is that now a wide range of possible designs and operating modes can be investigated and searched for their optimum cases.

This book is concerned primarily with digital simulation of chemical plant for the purposes of steady state process analysis. It introduces and explains the techniques involved and points out the value of such an analysis through a real example, by developing in detail a complete digital simulation of an existing sulphuric acid plant, using a particular simulation language called PACER. Inevitably this requires the use of much conventional chemical engineering, especially where it is being shown, in the middle chapters of the book, how digital models of the individual units making up the plant are constructed. The core of the work lies, however, in the earlier chapters where the methods used to link individual models into a complete simulation are described. It is here that it is seen that the approach needed for the simulation of a complex of plant is necessarily more ordered and disciplined than is common in process design, and that this quantification of what is usually done intuitively should be used more often in design.

The book is well planned, well written, sensibly arranged and supplied with clear diagrams. Several of the authors are known for their work in other fields of chemical engineering and it is significant of the importance of this kind of process analysis that they have got together with a chemical company and a computer manufacturer to produce this excellent result. I consider that this is an important textbook not only because of its useful contents but also because it in effect suggests that this subject, up to the present time the preserve of specialists, should now become a familiar procedure to all chemical engineers.

W. SMITH

Strengthened Solids

Strengthening Methods in Crystals. (Elsevier Science Series.) By A. Kelly and R. B. Nicholson. Pp. 627. (Elsevier: Amsterdam, London and New York, 1971.) £12.50.

MANY of us, I suspect, look at edited books with suspicion, since far too often they lack a systematic approach or seem out of balance, especially when the editors are not contributors. This book avoids these pitfalls and no doubt benefits from the fact that the editors are recognized authorities themselves in the field of strengthening mechanisms in solids. They have contributed chapters themselves and the book is given coherence by the informative introductory and summary texts that they have written, which set the theme and mark the achievements.

The book, which comprises some nine main chapters (more than 600 pages) all written by authors of considerable standing, is aimed principally at specialists in the field. The first chapter, entitled "Dislocation-Particle Interactions", which takes up one-fifth of the book and is written by L. M. Brown and the late R. K. Ham, is a clear and detailed exposition of present understanding of the ways in which hard and soft particles in a matrix can strengthen a solid. There follows a very informative account by M. F. Ashby of deformation mechanisms in two phase alloys with phases of differing yield stress. The chapter by N. S. Stoloff deals with the strength of ordered crystals and intermetallic compounds, and J. D. Embury deals with strengthening by dislocation substructures in the sixth chapter. The interesting account by J. W. Christian on "The Strength of Martensite", in the fifth chapter, reflects the advances in the knowledge of the behaviour of dislocations in alloys. Precipitation strengthening of ceramics is covered by G. W. Groves in the seventh chapter, in which, due to the nature of ceramics, the effect of particles on fracture behaviour is introduced.

During the past decade there has been a tremendous upsurge of interest in fibre reinforcement, and A. Kelly (an editor of the book) introduces this topic by dealing initially with the conditions in which fibre and matrix interaction results in matrix strength modification and leads on to the well established "mixtures rule" for strength where the interaction is less apparent and a major preoccupation is with toughness mechanisms.

The book is rounded off by two chapters by G. J. Davies and R. B. Nicholson (an editor of the book) respectively, which deal with the development of strong microstructures from the melt and the solid state. These interesting chapters show in some measure the extent to which understanding and experience (technology) can be rationalized.

The emphasis in the book is on metals, ceramics and their alloys; polymers get only a brief mention. One is tempted to say that a chapter on polymers would have been attractive, but its absence in no way detracts from the scientific value of the book. The individual authors cover their subjects comprehensively and in depth, perhaps inspired by the editors' own efforts. The book demonstrates very strikingly, I feel, the tremendous advances in our knowledge in this area that have taken place during the past fifteen years or so; this progress has been facilitated by the development of electron microscope techniques, which have led to such fruitful microstructural investigations. These advances have also brought maturity into the subject insofar that discussions of strengthening mechanisms are less polarized, as demonstrated, for example, in the conclusions to the chapter by Brown and Ham, where it is made clear that the contribution of various mechanisms, such as mechanical strengthening, order strengthening and so on, depends intimately on the alloy system under investigation.

In summary, the book, which is well produced and contains microstructural illustrations of a high standard, will be of great interest to experts in the subject and will find its way into all the relevant scientific and technical research libraries. I suspect personal purchase by working scientists will be inhibited by the rather disturbingly high price of £12.50.

J. E. BAILEY

Spectral Analysis

Analytical Spectrometry. By L. de Galan. Pp. viii+279. (Adam Hilger: London, September 1971.) £6.

THIS book is based on a course "intended for the general analytical chemist" and is an updated version of the 1969 Dutch edition. The author is at the Technische Hogeschool, Delft.

The word "spectrometry" is used in its most general sense and includes mass spectra as well as the spectrum of electromagnetic radiation from γ-rays to mm waves. More or less all "spectrometric" methods in general use for structural, qualitative and quantitative chemical analysis are included—molecular absorption (ultraviolet to infrared), atomic absorption and emission spectra, X-ray absorption and fluorescence, γ-ray emission of elements activated by neutrons, crystal structure by X-ray diffraction, and nuclear magnetic resonance spectroscopy. Notable omissions—presumably considered to be in insufficient general use—are Raman spectra, electron spectroscopy and Fourier transform spectroscopy. Electron paramagnetic resonance receives only very brief mention.

The principles of each type of spectrometry considered are very carefully set out, commencing with the background theory and leading on to the instrumentation necessary to make use of the general method. It is always difficult for an author to decide where to start. In this case the treatment is so elementary at the beginning of each section that one might think the book is intended for those who have almost no knowledge of physics and have not met even the laws of refraction nor the term "refractive index". On the other hand, a good facility in algebra and calculus is assumed. Such readers will be able to follow the book but will have mental indigestion before they have finished reading any one section. There must, however, be many who are experienced in some types of spectrometry—perhaps ultraviolet absorption and emission spectra—and who would like to consider the possibilities of some of the newer methods and they will find this book invaluable.

In general the book is written so that statements are very clear and precise. Some of the criticisms on detailed points which one has noticed may be mentioned. The use of the phrase "continuum spectra" in place of the usual "continuous spectra" can be a little irritating. The author asserts that numerical wavelengths should always be the value in vacuum, whereas wavelengths in air at STP are normally used; the former is perhaps more logical although this means that the first two Balmer lines for hydrogen are given as 658 and 487 nm, instead of the usual 656 and 486 nm; but he is inconsistent and in Fig. 2.2 sodium wavelengths in air are indicated. A problem on page 42 asks for the quantum numbers of the outer electron of aluminium. This is not a fair question; from what he has been told, the reader will "guess" the right answer. But he will then have the impression that he can deduce the answers for the ground states of other atoms—which is certainly not true for the heavy atoms!

At the end of each chapter is a useful list for "further reading" together with an assortment of problems carefully designed to make the reader think. To summarize, any analytical chemist anxious to widen his knowledge of spectrometric methods will find it very useful to have this book on his shelf.

G. F. LOTHIAN

Polymer Science

Textbook of Polymer Science. Second edition. By Fred W. Billmeyer, jun. Pp. xiv+598. (Wiley: New York and London, June 1971.) £7.50.

THIS textbook is a revised edition of that produced almost ten years ago. It comprises five sections dealing respectively with characterization of polymers, structure and properties, polymerization, properties of commercial polymers and polymer processing.

The characterization section serves as a brief introduction also, reminding the reader about intermolecular forces and bonds. Polymer solutions are dealt with in general, by stating the conclusions of theoretical studies and then applying them. This too is the case for measurement of molecular size and shape and for analysis and testing, this latter part devoted to physical methods.

The concepts of regularity and order are developed in discussing morphology, rheology and the relationship of physical properties to structure. Here again, the approach is readably descriptive, basic mathematical theory being referred to and results stated and used.

The section on polymerization deals with the chemistry, mechanism and kinetics and covers condensation, free radical addition, ionic, coordination and ring opening processes. This is extended to deal with the more complex situations which develop when copolymerization systems are studied.

A useful part of the book is devoted to commercial polymers, where cost and performance have to be balanced and where minor variants of the main polymer may have important uses in speciality items. More technological details such as plasticization and stabilization are dealt with here, and the thermosetting resins which do not fall easily into earlier more fundamental chapters.

The shorter final section deals descriptively with polymer processing and includes moulding, extruding, blowing and spinning, together with a brief mention of vulcanization.

To cover an extensive and advancing area of science and technology in detail in a single volume is clearly impossible, and in the present textbook the author has pruned away much of the detailed theory. The emphasis remaining is chiefly on a fairly descriptive level, showing what can be achieved by applying the results of theory to understanding complex polymer systems and relating these to the end technology.

This is a very readable book which can be recommended to student and practitioner alike, the former gaining a preliminary insight into this fascinating field of study and the latter having his horizons widened painlessly. The illustrations are good, many useful tables are provided, and the text is well referenced.

JAMES C. ROBB

Fast Reactions

Fast Reactions. By David N. Hague. Pp. viii+159. (Wiley Interscience: London and New York, July 1971.) £3.

DURING the past twenty years the accumulated knowledge concerning rapid reactions, that is, those which have half-lives of less than a second, has grown enormously. So much so that "fast" reaction kinetics is now an established and indispensable part of chemistry and biology. Although there have been a great number of research papers and reviews published in this field, so far there have been few textbooks. The author states in the preface that this book was written as an attempt to bring to the attention of the general chemist or biologist some of the excitement experienced by those working on fast reactions, who are continuously developing and improving their techniques, thereby revealing interesting new information concerning chemical reactivity. Since fast reaction applications are so wide ranging, it is hardly surprising that in a book of this size the author seems to have been exceedingly selective in his attempts to convey an impression of significant advances. It is questionable whether his treatment which often only scratches the surface in one or two places is likely to achieve his declared aim.

The first half of the book is devoted to a fairly comprehensive description of the various experimental techniques which have been developed for studying fast reactions. A brief outline of flow methods is followed by a discussion of large perturbation methods including flash photolysis, pulse radiolysis and shock tube methods. A nanosecond laser photolysis system is described but there is no mention of picosecond lasers. Chemical relaxation methods which utilize a single small perturbing pulse are dealt with in some detail but the treatment of those based on the use of periodic disturbances is much briefer. The author's treatment of competition methods based on nuclear magnetic resonance, electron spin resonance, fluorescence and polarographic measurements which are covered in less than twenty pages requires a great deal of background knowledge which even industrious senior undergraduates are likely to find somewhat exacting. However, research workers in other areas of chemistry may find the concise treatment to their liking.

The second half of the book is devoted to selected examples of reactions which have been studied by rapid reaction techniques. In the third chapter proton transfer reactions and the reactions of the hydrated electron are discussed in some detail and several useful tables of elementary rate constants are given. This chapter concludes with a *résumé* of recent results and theories concerning metal complex formation. The final chapter gives some indication of advances concerning rapid reactions in biological systems with considerable emphasis on enzyme reactions together with comments on the role of metals and nucleic acids in biology. At the end of each chapter a short list of useful references is given; in addition there are some problems on the second and third chapters.

The book is well written and produced. One doubts, however, if it is likely to be preferred to previous textbooks which act as an introduction to the study of the kinetics of fast chemical reactions. In spite of this, most libraries will probably want to buy this concise and thoroughly readable book.

F. WILKINSON

Inorganic Reactions

Inorganic Reaction Mechanisms. Vol. 1. Senior Reporter J. Burgess. Pp. xv+338. (The Chemical Society: London, June 1971.) £7.

SURVEYS of recent work are a valuable activity, of long standing, within the Chemical Society. The annual reports contained articles which, broadly speaking, fell into two classes. There were comprehensive reviews, covering all work in a given area. Much rarer were occasional masterpieces in which selection and critical evaluation of recent trends were keynotes.

This inaugural specialist report on mechanisms of inorganic reactions is of the former kind. It contains a full though rather uncritical survey of relevant literature from January 1969 to August 1970, with no obvious omissions. There are extensive tabulations, particularly in the sections on oxidation.

Some errors have been missed by the proof readers. This is not too distressing because the production of these volumes is gratifyingly rapid. There are, however, several perpetuations of error, which are deplorable in a publication of the Chemical Society—nomenclature for optically active compounds is antiquated; the effect of acid on the aquation of halo-complexes is called, very inexactly, catalysis.

Many opportunities to resolve controversial points or to help generalizations to emerge have been burked. For example, the bare statement is made about $[Co(C_2O_4)_3]^{3-}$ (page 200) that, "contrary to earlier suggestions that all twelve oxygen atoms exchange, a thorough investigation has shown that only six exchange with solvent oxygen". This implies that the earlier report is wrong. That work was done at a higher temperature, however, and, furthermore, the experimental graphs in the second report show that, even at the lower temperature used, slow exchange beyond six oxygens does occur. The two reports surely reflect the existence of two routes for exchange.

Apart from the last chapter on organometallic systems, which includes an interesting survey of new reactions, mechanism and kinetics (in spite of a disclaimer) are treated as synonymous. If we instead agreed with Nyholm that kinetics:mechanism=fact:fiction, and if we further accept that this year's science fiction may be next year's frontier of research, future volumes of this series might usefully redress the balance between kinetic and other aspects of mechanism.

R. D. GILLARD

Artificial Intelligence

Artificial Intelligence and Heuristic Programming. Edited by N. V. Findler and Bernard Meltzer. Pp. 327. (Edinburgh University: Edinburgh, August 1971.) £6.

THE first NATO Advanced Study Institute on Artificial Intelligence and Heuristic Programming was held in Italy in August 1970. Fourteen leading artificial intelligence (AI) research workers were invited to lecture on the states of the art and science of AI to an audience consisting mostly of informed students. This book contains a set of papers, based on those lectures. A comprehensive index is included in the book.

Collectively, the papers embrace most of the major themes in current AI research—computational logic, problem solving and problem solving compilers, natural language processing and models of cognitive processing. The papers are well written and as a book cohere through the noticeable consistency with which individual authors have balanced the tutorial and research-report content in their papers, due no doubt, to the editorial effect of the audience in the summer school.

The paper by Robinson on building deduction machines, and related remarks in the paper by Raphael on the "frame problem", contain perhaps the clearest statements of these topical issues to appear in the literature. Robinson's paper ends with remarks about the need to find upper and lower bounds on the amount of work required to carry out specified tasks, a theme related to Meltzer's discussion of efficiency in proof procedures. Needless to say, we are a long way from being able to formalize efficiency in even the simplest of tasks. In fact, it is doubtful whether at present we can indicate how a calculus of efficiency (which necessarily must work over some procedure specification) might be formulated. Meltzer's contribution to this important issue embraces a framework for examining proof procedures which he uses to sharpen the relationships among incompleteness, completeness and heuristic. He gives a lucid account of proof procedures as composites of inference systems and search strategies and pinpoints the intrusions of appeals to human performance.

At the other end of the spectrum of concepts which motivate AI work, Kochen, in a wide ranging paper, discusses cognitive learning processes. He rejects the current trends in AI towards better heuristics, powerful deductive inference schemes and so on, as being an entirely inappropriate path to an understanding of cognitive learning. He proposes and argues for a model which allows him to order hierarchically what could be meant by knowledge, utility, comprehension and wisdom and within which specificity is lent to psychological terms such as understanding, awareness, intention, thought and so on. This rather broad philosophically oriented exposition is supported by a mathematical model and some suggestive implementation results.

The natural language area is covered by contributions from Lindsay, Simmons and Palme. In Lindsay's paper we find another extremely clear statement of an important AI concept—the influence of context on computation. Lindsay reports on the design of a natural language learning system based in part on this principle. Palme takes a broader look at the field and includes a review which unfortunately loses a little through predating Winograd's work at the Massachusetts Institute of Technology. The paper contains a useful annotated bibliography. Conceptually allied to the semantically oriented approach to linguistic processing, Clowes's work on picture analysis invites us to consider the semantics of pictures. In his paper he argues cogently for the need to incorporate within a picture processing system the structure of what is depicted.

The development of heuristic search strategies and the means by which they can be influenced by specific problem contexts is an AI study area of considerable importance. Most AI programmes have search problems. In two complementary papers, Sandewall and Michie give a thorough discussion of the achievements in this area. Sandewall anatomizes the tree/graph type of search mechanisms, giving some well thought out terms for referring to various salient features. Michie is more concerned with the general problem of plan formation, which he presents from the standpoint of the heuristic search paradigm. He points out that only simple plans (that is, plans derived from fully specified input states and operator effects) can be made from existing heuristic search mechanisms alone.

Generalized problem solving techniques take their most convincing form when integrated into an acceptor for some language. This notion, together with the associated problem of designing declarative languages, leads to what are now called problem solving compilers. The book contains an informative paper by Elcock on this topic and a couple of related papers, one by Findler on the application of a new programming language, and one on a language for a game playing system by Pitrat.

Given that this book is essentially the proceedings of a symposium, it contains a larger than usual complement of high quality papers. With the treatment of the material leaning towards the tutorial, it will interest many "fringe" workers as well as the more obvious audience of AI students.

R. B. STANTON

Polyatomic Molecules

Rotation–Vibration of Polyatomic Molecules: Higher Order Energies and Frequencies of Spectral Transitions. By G. Amat, H. H. Nielsen and G. Tarrago. Pp. vi+441. (Marcel Dekker: New York, April 1971.) $19.50; £9.30.

THE systematic study of the rotation–vibration spectra of polyatomic molecules dates from the classic 1936 paper of Wilson and Howard. The early work was brought to an initial level of completeness in a much used review article by Nielsen in 1951. However, it became apparent that higher-order contributions had to be considered to account quantitatively for observed spectra. For this reason a systematic treatment of the higher-order terms was undertaken in a series of papers begun by Goldsmith, Amat and Nielsen in 1956. The present volume is essentially a revised and unified presentation of this series, together with later additions from theses of students belonging to the Amat–Nielsen school.

Like the original papers, the book is devoted chiefly to the mechanics of the perturbation calculations, with little reference to actual spectroscopic observations or methods of interpreting them. The Darling–Dennison molecular Hamiltonian is introduced without derivation and is expanded as a power series. Two successive contact transformations are performed in order to eliminate as far as possible terms which are off-diagonal in the vibrational quantum numbers. This twice-transformed Hamiltonian is then in a convenient form for fitting to observed spectra. The notation required to keep track of the various contributions becomes quite elaborate, and numerous tables are given to relate the coefficients in the twice-transformed Hamiltonian to the basic molecular parameters. Extensive tables of matrix elements of the twice-transformed Hamiltonian are also given, with particular emphasis on molecules with three or four-fold axes of symmetry and on linear molecules. Most of the book (more than 300 pages out of 441) actually consists of tables either of matrix elements or of algebraic relations.

This monograph is obviously not designed for beginners. Workers interested in the finer details of microwave and infrared spectra may find it convenient to have this collection of results by a well known school brought together for ease of reference. However, I would have liked to see more consideration of the problems arising in the practical application of the formulae.

The book itself is reproduced by a photo offset process from a typed text, with most of the tables and special symbols drawn by hand. The result is perfectly clear, but seems excessively expensive.

J. K. G. WATSON

Optical Methods

Modern Optical Methods in Gas Dynamic Research. Edited by D. S. Dosanjh. (Symposium held at Syracuse University, New York, May 1970.) Pp. xii+295. (Plenum: New York and London, 1971.) $16.24.

THIS volume brings together sixteen papers contributed to a symposium on progress in gas dynamic research by optical methods held early in 1970. They cover a wide and somewhat heterogeneous range of topics including shock tube spectroscopy and other radiometric methods in non-equilibrium flows; temperature errors in plasma diagnostics and their possible effects on absolute transition probabilities; impurity measurements in the expansion tube; diagnostics based on refractive index with particular stress on dispersion and hook interferometry; some optical diagnostic techniques involving lasers for the production of plasma, for holographic interferometry, for (Thomson) scattering; a summary of recent research on continuous wave chemical lasers; excitation by tunable lasers; and recent studies of the CS_2/O_2 combustion laser.

In view of everyman's struggle to avoid being bowled over by the information explosion, it is unfortunate that the title of the volume appears to imply that it is a textbook or even a comprehensive review. There seems no good reason, other than sales promotion, for not having used the title of the symposium itself, though even prefacing the present title by "some" would have helped to increase the signal-to-noise ratio. As the proceedings of a symposium, the volume contains a very high proportion of valuable papers, as may be expected, since the contributions all seem to have been invited and the contributors include many distinguished names. As a collection of review papers purporting to cover the entire field, however, the book falls between two stools. It is too diversified and expensive to encourage the individual worker in any one of the disciplines covered to buy it, yet it is very far from being a comprehensive review. For example, in the field of refractive index diagnostics, there is no mention of perhaps 80 per cent of the new laser interferometric methods, the application of Schlieren methods is touched on without any reference to the problems arising in their use with laser sources, interference using Doppler-shifted light is not even mentioned, scattering measurements are concentrated around one particular regime, and so forth. As against this, no less than three papers deal with various aspects of dispersive (hook) interferometry. Presumably the coverage is due to the selection of contributors, and the form to the instructions issued to them. A useful comment on this is given by one of the contributors who concludes as follows: "The preceding text was written in a format primarily intended for oral presentation at the symposium, without specific citations. For the record, and the interested reader, some references weighted towards the author's work and without regard for completeness or priority are given. . ."

None of this is a criticism of the individual papers, most of which are excellent and a few of which are indeed comprehensive reviews of the fields indicated by their particular titles. The contributions on chemical lasers and on hook interferometry perhaps deserve special mention. The comments concern only publication policy and, since this invariably succeeds, are a futile gesture anyway; if we cannot obtain relevant reprints from individual authors we shall just have to pay $16.24 for the entire volume.

F. J. WEINBERG

Aromaticity

Aromaticity and Anti-aromaticity. (International Symposium held at Jerusalem, April 1970.) Edited by Ernst D. Bergmann and Bernard Pullman. Pp. 398. (The Israel Academy of Science and Humanities: Jerusalem; Academic: New York and London, July 1971.) $21.50; £10.05.

"WHERE have we anything to do with Mechanikal Chymistrie that hath outstript the other Sects of Philosophy by her multiplied real experiences?" asked the Puritan, Noah Biggs, in his *Chymiatrophilos* of 1651, addressed to the Parliament of England. The present volume of quantum mechanical and physical organic chemistry devoted to the subject of aromaticity would doubtless have gratified Biggs, but he may well have felt that a subsidiary project in his grand design for the advancement of learning was left incomplete. "Where," he asked further, do we have "a Review of the old Experiments and Traditions, and casting out of the rubbish that hath pestered the Temple of Knowledge?"

The thirty-four contributions to the symposium held in Jerusalem in 1970 circle round the elusive concept of aromaticity with new calculations, new measurements and new syntheses, each attempting a closer definition. The new studies lead, however, to a fragmentation of the concept and generate overlapping sub-classes distinguished more perhaps by their prefix, pseudo-, anti-, quasi-, non-, homo-, and even pseudo-anti-aromatic, than by their content. As Heilbronner observes (page 22), many molecules might be termed "schizo-aromatic", for the allocation of a molecule to a sub-class depends on the particular chemical or physical property or theoretical measure used as a criterion. A possible exception may be the paradigm case of benzene, the arche-aromatic (Lloyd, page 89).

Historically, the concept of aromaticity has played a major role in the development of physical-organic and π-electron chemistry. Beginning as a loose description of compounds with an agreeable aroma, "aromatic" became, with Kekulé (1865), an archetectonic term describing the molecular structure of six-membered ring compounds related to benzene. Classically molecular structures were proposed chiefly to account for chemical reactions, as opposed to physical properties, and aromatic substances came to be primarily characterized by their substitution reactivity (Robinson, 1925). Quantum chemistry introduced the new criterion of electronic structure in Hückel's rules (1931) and emphasis shifted to the electronically-dependent physical properties. Studies of these properties have undermined the old distinctions and introduced new ones which are far from concordant among themselves. The proceedings of the 1970 Jerusalem symposium suggest that the concept of aromaticity is a Wittgenstein ladder which chemists have climbed and now, on reaching the top, should throw away.

S. F. MASON

Air Pollution

Air Pollution Control. Part 1. (Environmental Sciences and Technology: Wiley Series of Texts and Monographs.) Pp. ix+451. (Wiley: New York and London, August 1971.) £9.50.

THIS is not a book on air pollution control, it is a set of seven disparate review articles on equally disparate subjects, bound up together. The reviews on the collection of particles by fibre filters, forty pages, and condensation effects in scrubbers, fifty-two pages, are both theoretical accounts with notes on experimental work to back up the theory, but little about practical applications. Both could be quite useful to a newcomer to research and development in these narrow fields, for the authors were allowed a reasonable space in which to expound their subjects and used it well. By way of contrast the author of the review on the dispersion of pollutants attempted valiantly to deal with this complicated and difficult topic in thirty-four pages. The rather breathless rush towards the end prevented adequate treatment of what promised to be the most valuable part of the chapter. In contrast again, the review on electrostatic precipitation occupies 110 pages on "updating prior surveys . . . with the emphasis on physical principles and predictive methods rather than on equipment and empirical descriptions". It ends, however, with a useful and wise, although all too short, discussion on applications, costs, difficulties and so on.

The chapter on the formation and control of oxides of nitrogen is a well balanced review of the role of these substances as air pollutants, as is also that on the control of internal combustion engines. This latter gives essential practical details often lacking in some accounts of motor vehicle problems.

The remaining article, on the control of sulphur emission from combustion processes, is a very mixed bag indeed, and I was left with the uneasy thought of what the reader could conclude from it as to the present state of the art in these fields. While a great deal of accurate and useful information is presented it is mixed up with the pipe dreams of inventors of an earlier generation and no key to the maze is given. In some instances the information is inaccurate in fact, in others by implication. For example, it is stated that a Howden–ICI cyclic lime process was installed at Fulham power station in 1935 and a flow diagram and explanation of the method is given. It is not stated that the plant was shut down in 1939 and that the process is as dead as the proverbial dodo. The fact that, later in the chapter, the author copies out a detailed table of costs raises suspicions that he is not himself aware of the true position. The Fulham–Simon Carves ammonia process is described and it is stated that the North Wilford plant, commissioned in 1957, "handles the combustion waste gases from . . ."; it does not, as it was shut down some ten or eleven years ago. This sort of thing destroys confidence.

Looking back at the book as a whole, all the chapters contain excellent collections of references, and some of them consist, in effect, of useful sets of notes on these references. As such it has a certain real value, but a value that is very small indeed in relation to the price of £9.50 for the 451 modest sized pages. Perhaps for the first time I have understood my American colleagues who try to buy all their private technical books from British publishers in the United Kingdom.

S. R. CRAXFORD

Time Past

Geological Time. By J. F. Kirkaldy. (Contemporary Science Paperbacks No. 46.) Pp. 133. (Oliver and Boyd: Edinburgh, April 1971.) 37½p.

BEGINNERS in geology often find difficulty in comprehending the enormous span of geological time. A million years is difficult to appreciate. But since an understanding of the duration and significance of time intervals is important in most branches of geology, the sooner that these figures are understood the better. What the author has done has been to explain in simple language why time is so important in geology and how it is measured.

The first chapter is a brief historical survey of ideas of the age of the Earth, showing how ecclesiastical dogma was dominant up to the nineteenth century.

Perhaps more significantly, however, it was the formulation of geological concepts, the laws of superposition and principle of uniformitarianism, which in the end led to ideas of duration of processes and hence to a relative time scale. Professor Kirkaldy stresses the importance of the early workers in these fields and goes on to demonstrate how the next step, of correlating strata by their included fossils, came about. Thus, with these fundamental principles, workers were able to erect stratigraphic successions and, in doing so, make relative datings of beds. The added complications of breaks and modifications (for example, unconformities and orogenies) in the succession are explained and their significance in working out a time sequence is demonstrated.

Following on from this, Professor Kirkaldy surveys the methods by which estimates of elapsed time have been drawn up. Thickness of sediments and rates of sedimentation as methods, salinity increases, palaeontology and evolutionary rates, and the rate of cooling of the Earth are discussed at length. All give markedly different ages to the same rocks.

After this survey of relative methods of age determination the book continues with an introduction to dating using radioactive isotopes. This is an exceedingly useful chapter, the physical concepts behind the determination being clearly set out and each of the principal isotope ratio methods explained. The specific advantages of each method are given together with the rocks, or more properly minerals, on which it is best used.

In 1913 Arthur Homes was one of the first to draw up an absolute time scale from data available. Scales were modified as new dates became available and as more precise techniques for isotope measurement were invented. In this part of the book the more problematical determinations of Pleistocene and Recent dates are examined and the reliability of dates throughout the stratigraphic column is pointed out. Methods of determining time sequences in metamorphic and highly folded and faults areas are indicated, and this has a bearing on the account of Precambrian time which follows. The book ends with a discussion of the age of the Earth and the solar system, and the significance that Moon dates have on this.

This is certainly a book which all beginners in geology should read, and it will provide a valuable refresher course to their more experienced colleagues. If isotope measurements are to be used it is important that geologists understand how they are calculated and how reliable the dates derived are, unless he is to accept them blindly.

J. R. V. Brooks

Soil Analysis

A Textbook of Soil Chemical Analysis. By P. R. Hesse. Pp. xxiii+520. (John Murray: London, April 1971.) £7.50.

This book is designed to provide a course on soil chemical analysis and will prove to be a valuable text both for teachers and students. Practising soil chemists should also find much of interest in it. The two introductory chapters, covering the purpose of soil analysis, precision and accuracy, preparation of samples and the interpretation of results, are excellent; the author's critical awareness of the problems involved should help to dispel "the myth of soil analysis being the answer to the farmer's problem". The remaining sixteen chapters are given to a particular element, group of elements, or property of soil, and cover most chemical topics of interest to a soil scientist. The chapter on waterlogged soils is an innovation that should stimulate work on an important but neglected subject.

Most chapters have a short introduction, rather more extensive for lesser known topics, then a section on the background and theory of the determination, and finally practical details for recommended methods. A number of different approaches are described for most problems, covering the literature fairly thoroughly, and making the book a more comprehensive guide than has been available hitherto.

The analytical methods for which detailed instructions are given use chiefly simple apparatus so that they are well within the scope of the average soil laboratory; this should particularly commend the book for situations where resources are limited. Sophisticated instrumental methods are mentioned where they can make a contribution, but the reader is referred to other publications for details. Simple diagrams of apparatus, and flow sheets for some of the complex determinations, are welcome aids to clarity. Appendices contain references, bibliography and useful information on standard solutions, conversion factors and so on, and there is a full subject index.

Analysis of soil is a very different proposition from conventional chemical analysis, for the total amount of an element or compound is only rarely required. The need, rather, is for the proportion that is likely to be involved in the process under study, be it pedogenesis or plant nutrition. An essential prerequisite for effective procedures is thus an understanding of basic soil chemistry, and it is gratifying that one of the prime aims of this text is "to narrow the gap between the theory of soil chemistry and the manuals of soil analysis". That this gap still seems to be rather wide in some cases is due not only to the complexity of soil chemistry, but also to the uneven treatment given here to the underlying theory, particularly the more physicochemical aspects. There are also a number of misleading statements that undermine the book's authority on general soil chemistry. The author is clearly on safer ground when dealing with analytical procedures.

Rapid advances in this important practical subject will ensure that a second edition is required eventually. This should provide the opportunity to remedy some blemishes in an otherwise excellent publication.

B. W. Bache

Analysis of Sediments

Procedures in Sedimentary Petrology. Edited by Robert E. Carver. Pp. xiii+653. (Wiley: New York and London, June 1971.) £11.75.

This book is intended as a guide to the standard procedures for measurement and analysis of sediments. There are six principal sections which deal with the analysis of sedimentary structures—size, grain, texture, mineralogy and chemistry. Several authors contribute chapters to these sections and the coverage of subject matter is fairly complete. There are chapters on thin section making, heavy mineral separation, staining, point counting, peels and impressions, X-ray photography, X-ray diffraction, porosity and so forth.

Size analysis is well covered with a useful table of sieve data, sieve analysis, pipette analysis and related methods of sedimentation analysis (including the rapid sediment analyser using a water pressure transducer). Instrumentation for electronic grain size measurements in thin sections is described and a mathematical treatment of size distribution is followed by an examination of grain size shapes and grain surface textures. Scanning electron microscopy is used to identify the effects of littoral, aeolian and glacial environments on the surfaces of grains. The sections on mineralogical analyses give a good account of gravity separation, but magnetic and electromagnetic methods are not adequately described, nor is any reference made to the "micropanner" which is often a useful tool.

The chapters on X-ray photography are particularly interesting and more use should be made of it in petrology. The chief difficulty is the general lack of suitable medical/industrial-type X-ray units in most geological departments, although excellent X-radiographs of rocks can be obtained from a small apparatus employing a ^{125}I source (Weiss, *Amer. Assoc. Petrol. Geol.*, **50**, 1507; 1966). There is a thorough treatment of optimum sample thickness and other parameters, together with descriptions of the more special techniques of stereo X-radiography which is of considerable value in studies of three-dimensional texture and of fluid movement in sediments.

The section on chemical analysis might be misleading because it only deals with the determination of carbon (as total organic carbon) and carbonate-carbon, followed by a chapter on the measurement of *E*h and *p*H. The techniques suggested for determining organic carbon are standard ones, including wet and dry combustion methods, the results of which are compared. Dry combustions were made on commercially built Coleman and Leco C-H analysers. In my experience, analyses of organic carbon in carbonate-rich sediments tend to be erratic when they are calculated by difference between separate total carbon and carbonate-carbon analyses. The single sample method (Shaw, *J. Soil Sci.*, **10**, 323; 1959) is usually more reliable.

The book constitutes a valuable laboratory guide and source-book on the methodology of sedimentary petrology and has assembled a lot of widely dispersed literature. T. W. Bloxam

Biological Sciences

Biodevelopment

Molecular-Genetic Mechanisms of Development. By Zhores A. Medvedev. Translated from the Russian by Basil Haigh. Pp. xiv+418. (Plenum: New York and London, 1970.)

It is part of the current biological faith that the advances in genetics and molecular biology will provide the means to understand embryology. Some molecular biologists are turning to developmental biology, and this is only right, for developmental biology occupies a key position in biology: it can be seen as the means whereby genetic information is expressed in terms of functional cellular patterns and organized forms. It provides the link between genetics on the one hand, and morphology and physiology on the other. What is not at all clear is the level at which rapid progress is to be made and I remain to be persuaded that, at this stage, studies at the molecular level will always be the most productive. While it might be true for the control of gene action and protein synthesis, a contrary argument might be made for such aspects of development as pattern formation, where the cellular basis is not understood. And even for gene action it seems that some of the striking recent advances have come from cell biology, namely nuclear transplantation and cell hybridization.

The book does not live up to its exciting title and, however good a molecular geneticist the author may be, he gives little indication of having insight into the problems of development. For him it seems it is nothing more than gene activation and that this is best understood in terms of thinking from bacterial models. Most of the book is concerned with molecular biology and biochemistry. It starts with DNA and protein synthesis and then goes on to virus reproduction. The emphasis here and elsewhere is on molecular genetics and, for example, while virus assembly is seen as a morphogenic process it is not treated as such. Self-assembly and its associated problems along Caspar-Klug lines is barely mentioned. This is followed by an account of induction in bacteria and chromosome replication.

Material more relevant to development is considered in the chapters on chromosome structure and function, and changes in proteins and nucleic acids during development. While they contain a great deal of data, they form rather unsatisfactory reviews because of the lack of an adequate conceptual framework. Biochemical morphology, such as changes in enzyme activity of four enzymes during development, is as dull as the dullest traditional morphology. Also the style, perhaps due to translation, makes reading difficult: for example, "The issuing of programming instructions by the nucleus cannot be turned simply in time or in space (as in a certain type of symmetry), but it must conform to the actual morphological and physiological pattern of development, to the new conditions arising on account of the new relationships". The last chapters on the control of gene action are the most interesting but, because they were written in 1968, are somewhat out of date. Repetitive DNA, molecular hybridization, cell hybridization, recent work on nuclear transplantation are virtually absent and only receive brief mention in the last chapter written in an attempt to bring the book up to date. Cellular interactions, cell movement, polarity, determination, transdetermination, quantal mitoses, which are frontier regions of developmental biology, are just absent. This is classical molecular biology crudely applied to embryology. Perhaps the author, who is scholarly and very knowledgeable, is just too out of touch with current trends in the field.

Lewis Wolpert

Cells and Molecules

Advances in Cell and Molecular Biology. Edited by E. J. DuPraw. Pp. xv+308. (Academic: New York and London, July 1971.) $15; £7.

Protein Synthesis. Edited by Edwin H. McConkey. Pp. xi+298. (Marcel Dekker: New York and London, 1971.) $19.50.

The aim of each of these volumes is to provide reviews which will keep abreast of research on the rapidly expanding topics of cell and molecular biology. Each promises to be just the first in a series, future volumes of which will appear at unspecified intervals.

What distinguishes these series from the many others already available? *Advances in Cell and Molecular Biology* is related to DuPraw's book, *Cell and Molecular Biology*, on which it will build. One of the hazards of writing books on topics such as these is that they tend to become out of date so very rapidly. By editing a series, to which contributions will be made by many authors, DuPraw intends to keep up to date the ideas discussed in his book.

But the contributions to the first volume of this series are written at a level very different from the basic text to which they are supposed to relate. Each article consists in part of a detailed review of the author's own work, in part of a review of research in general. The readers of the series of reviews will presumably be very different from those who would read the original text.

How useful will the series be as a collection of reviews of this type? I must confess that my prejudice is that series of this nature serve little useful purpose, except for those who are themselves working in closely related fields; but such people are usually fairly well informed in any case. What is needed so badly is a series of reviews which can easily be understood by those not themselves indulging in research on the particular topic to be discussed.

There seems, indeed, little to distinguish this new series from the many other review volumes with which cell and molecular biology is served. The emphasis of the first volume lies with the chromosome itself. Each review is very detailed, so that the unitiated will find it difficult to follow the discussion. Each contains a number of references to be measured in hundreds rather than in tens; it will be a discerning reader indeed who can pick out the main lines of research from among them.

The aim of the series *Protein Synthesis* is to provide a critical evaluation of progress in research, both in eukaryotes and prokaryotes, and not merely to list recent data. The contents of the first volume are concerned with the synthesis of the polypeptide chain, the structure and function of the ribosome, and the charging of tRNA. Most of the articles take a historical approach.

In spite of the restricted area discussed, the individual articles, although in the main well written, do not relate well to each other. But the two articles on protein synthesis, in particular, are brief and come close to achieving the aim of a critical evaluation of the state of play. The other articles are longer, some of them tending to take a more definitive stance instead of keeping strictly to one theme. Nevertheless, on the whole this volume is better written than most such reviews and readers would do well to keep an eye open for future volumes. BENJAMIN LEWIN

Embryological Methods

Methods in Mammalian Embryology. Edited by Joseph C. Daniel jun. Pp. xv+532. (W. H. Freeman: San Francisco and Reading, July 1971.) £10.70.

MILESTONES in the development of mammalian embryology were the first sighting of mammalian eggs and pre-implantation embryos by Cruikshank in 1797 in the rabbit, and in 1890 Heape's successful transfer of fertilized rabbit eggs from one doe to another, which marked the initiation of experimental embryology in mammals. Fig. 1, based on the chronological distribution of references in Daniel's new *Methods in Mammalian Embryology*, illustrates graphically the steady rise in interest in the subject throughout the 1950s, leading to a formidable volume of work during the past decade. The decline in number of references since 1967 is an artefact: internal evidence suggests that most of the chapters were written before 1968, though some have been revised more recently.

It is intriguing to speculate why the subject took so long to get going, since few of the techniques involved require sophisticated modern equipment, and most of the 1960s work could as well have been done in the 1920s. The most important single technical advance was probably the introduction of antibiotics during the Second World War. This democratized culture techniques of all kinds, and opened the way for *in vitro* culture and experimental manipulation of mammalian embryos on a large scale. Even more important, perhaps, was the question of social incentive. As advances in medical science led in many parts of the world to a rapid increase in population, the necessity of fertility control was belatedly recognized. At the same time the reduction in infantile mortality due to infections highlighted the significance of congenital malformations. Reproductive biology, including mammalian embryology, has in consequence become a well endowed and fashionable subject, no longer sequestered in some corner of a university zoology department.

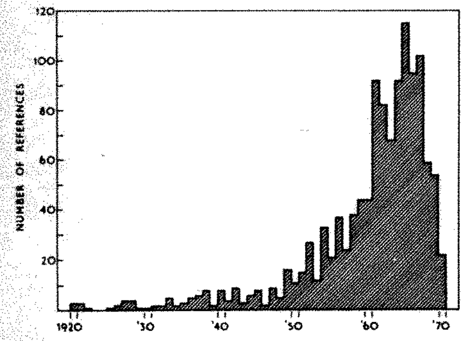


Fig. 1 Increasing interest in embryological methods, illustrated by the references given by Daniel in his book.

Methods in Mammalian Embryology includes four chapters on eggs and spermatozoa, one on fertilization, eight on egg storage, culture and transfer, four on experimental manipulation, including micromanipulation, three on biochemical analysis, five on electron microscopy, autoradiography, histology, cytology and fluorescence techniques, four on organ and cell culture, and six on implantation and placentology. Although not entirely up to date, it gives a good all-round background, and each chapter is written by an expert who has used extensively, in many cases pioneered, the techniques that he describes. Tips range from the esoteric (Mintz's use of ant cocoons as mouse-egg containers for histology—"we have collected especially good quality sacs in sandy soil under stones and wood in New Jersey"; Blandau's impressive array of instrumentation for observing and photographing ovulation and egg transport *in vivo*) to the homely (Dickmann's demonstration that rat eggs can be transferred, if all else fails, in tap water; Enders's injunction to take care that flushings "land in the recipient container rather than on your lab coat").

There are some sections that could be drastically shortened, and some curious omissions. No mention is made of human embryos and the techniques such as amniocentesis, ultrasonic analysis, laparoscopy and foetoscopy, which are increasingly used in their study. Nothing is said about irradiation or about culture of pre-implantation embryos in any species other than the mouse. Particularly in the chapter on egg storage, there are many general statements, without reference to species, which may prove dangerously misleading.

The index is good. It seems deeply ungrateful to carp when editor and authors have in many ways done such an excellent job, but if the volume had been half the size, half the price, and published two years earlier, it would have been more than twice as valuable.

A final word of warning. Although this book is a mine of useful information, it is no substitute for visiting a laboratory and seeing how things are actually done. ANNE MCLAREN

Regeneration

Regeneration of Liver and Kidney. (*New England Journal of Medicine.*) By Nancy L. R. Bucher and Ronald A. Malt. Pp. xiv+278 (Little Brown: Boston, Massachusetts; Churchill, Livingstone: Edinburgh, 1971.) £6.

IF a substantial portion of the liver of a rat or a mouse or a dog is surgically removed, the remaining fragment grows, rapidly at first and then more slowly, until it attains the approximate size of the original intact organ. Similarly if one kidney is removed, its partner grows to approximately twice its normal size. These parallel examples of compensatory growth or "regeneration" have been known for half a century, but the mechanisms involved are still very much a mystery. The *New England Journal of Medicine* recently published extensive reviews of liver regeneration by Dr Bucher and of kidney regeneration by Dr Malt. These have now been reorganized, expanded and brought up to date to form a short monograph. In the process the authors and their publisher have taken full advantage of the opportunities offered by publication in book form rather than in the cramped pages of a journal. The result is (like other volumes in the same series) attractive in format, typography and illustration. It contains a good deal of new material, and the old material seems to have been carefully revised. The style of the book is clear, concise and readable.

Though there is some difference of emphasis between the two parts of the book (kidney function being, for example, given more space than liver function), it is held together by the similarity in outlook of the two authors. Neither Dr Bucher nor Dr Malt has tried to provide a review of the sort which is a *catalogue raisonné* of everything which has been published in a given field. They have attempted instead to relate knowledge of regeneration in liver and kidney to the present understanding of protein and nucleic acid metabolism. Their introductory chapter is a summary, brief and austere but lucid and agreeably illustrated, of the relationship between chromosomes and protein synthesis. Of the 160-odd pages devoted to the liver problem, more than half are concerned with molecular biology in some way, and the same central theme is almost as dominant in the discussion of the kidney. The success with which the authors sustain their chosen approach is remarkable. Attempts to interpret biological phenomena in biochemical terms are common enough but they are seldom supported by such a command of general biochemistry. Moreover, some of the difficulty and some of the attraction of liver and kidney regeneration as a subject for research is that it does not lie clearly within the province of any recognized discipline. It was originally opened up by experimental surgeons, but it has since engaged the attention of zoologists, physiologists, biochemists and pathologists. It is a considerable achievement to have organized material from so many diverse sources around a single central theme.

The one weakness in an otherwise excellent book is the brief comparison of regeneration in the two tissues with which it ends. Like everything which has preceded it, this is concise and lucid, but it could with advantage have been longer. The authors are leaders in their respective fields. Many of their experiments have been marked by novelty of approach and extraordinary technical virtuosity. Having devoted 250 pages to describing the existing state of knowledge they might have allowed themselves more than three pages to discuss their conclusions. R. Y. THOMSON

After the Apple

Gravity and the Organism. Edited by S. A. Gordon and M. J. Cohen. Pp. ix+474. (University of Chicago: Chicago and London, September 1971.) £6.30.

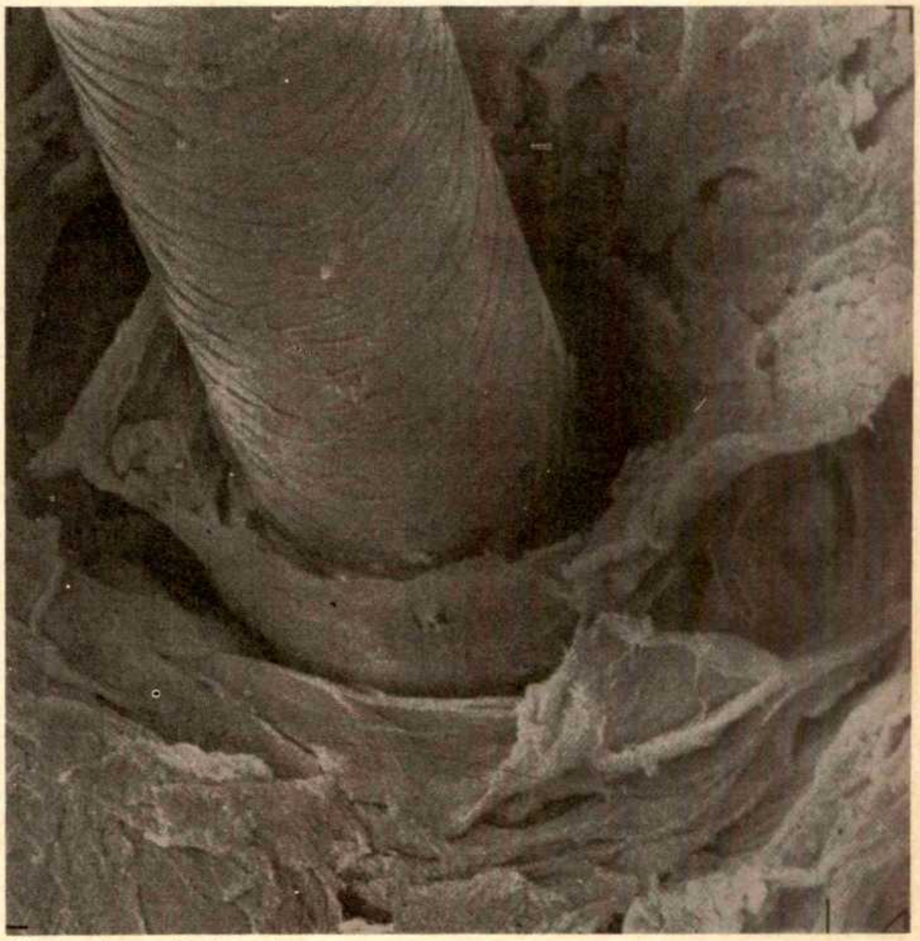
ALTHOUGH this book covers a diverse and important field of knowledge it will be known to people who work in it as tightly compartmented. Thus, a vertebrate biologist will be familiar with the statoliths of fish and mammals, their mechanical responses to acceleratory forces including gravity and the associated neural mechanisms whereby these responses are translated into appropriate movements or sensation. But this is only part of a much larger picture. His ideas will need to be enlarged; for instance, by reference to the work of plant biologists on the geotropic mechanisms of plants, and in a variety of other directions. For this there is needed a freer diffusion of knowledge between the compartment walls and much is done to achieve this by the compendium of up to date information, well balanced and handsomely presented, which is to be found in this volume. This comprises the texts of thirty-nine papers, together with the discussions relating thereto, which were presented at a symposium on gravity and the organism at Tuxedo, New York, in 1967. The contents have since been updated to 1971, the year of publication.

The meeting was sponsored by the Space Science Board of the US National Academy of Science with the support of the National Aeronautics and Space Administration (NASA) and attracted fifty-four participants. Twenty of the papers were from the United States and eighteen from European laboratories, including five from Great Britain. There was also a contribution from Japan. There is an excellent introduction by Dr A. H. Brown of the University of Pennsylvania, and summaries are provided by Professor O. Lowenstein of Birmingham and Professor A. W. Galston of Yale.

The resulting book is large; 470 pages are divided into seven parts, covering the reactions to gravity of plants (three parts), invertebrates (one part), and vertebrates (one part). There is also a large part (100 pages) devoted to gravimorphism in plants and animals. The final part contains an interesting summary of recent space studies.

The areas most familiar to me are those concerned with the functional anatomy and gravity sensing mechanisms of the inner ear of animals. These are dealt with by Gualtierotti of Milan and Lowenstein. They are of notable excellence and include an up to date summary of electron microscopic data. Other sections of especial interest are concerned with gravity susception by plants. This, according to some workers, would appear to involve mechanisms essentially similar to those of the animal labyrinth. Here, use is made of statoconia which by virtue of their high specific gravity are displaced by gravity, stimulate the underlying sensory cells and so initiate movements of the animal which are appropriate to its gravitational circumstances. Larsen of Bergen presents very clear evidence that in plants the part of the statoconia is played by certain high density elements which are judiciously categorized as "sedimentary particulates". According to the positioning of the plant with respect to gravity these particulates, in some cases starch granules —amyloplasts—will vary their position

Human Hair



The basal part of a hair of the human head. The epidermal surface is covered with leaf-like cells which, when peeled off, will form dandruff. (Magnification ×1,020.) Taken from *Atlas of Scanning Electron Microscopy in Medicine,* by T. Fujita, J. Tokunaga and H. Inou. (Tokyo: Igaku Shoin; Amsterdam, London, and New York: Elsevier 1971.) £9.00.

within the plant's cells and by acting on their walls in some way determine the occurrence and direction of the plant's growth. In a later section Edwards and Gray of Atlanta, Georgia, give a valuable account of the intracellular changes observed to occur when plants are exposed to chronic acceleratory forces up to 150*g*. Some of the findings are considered to support the view that the amyloplast granules of plant cells act as gravity receptors.

In the absence of structurally definable nervous or receptor elements large gaps in the argument remain to be filled. Here the evidence relating to the action of the hormone auxin and other growth regulating substances is highly relevant and the contribution of Wilkins of Glasgow is of much interest.

It seems right to say that all who concern themselves with gravity and its effects on living organisms will owe much to the organizers of this symposium. The publication of its records in the form of this book is a notable achievement in the dissemination of scientific knowledge.

C. S. Hallpike

Ions and Membranes

Ion Transport and Membranes—A Biophysical Outline. By A. B. Hope. Pp. 121. (Butterworth: London, March 1971.) £3.00.

The content of this book is not a great deal more than often found in a review article. It consists of just over a hundred pages which make up ten short and concise chapters. Although the text is limited it does adequately cover the basic theoretical concepts and experimental approaches which are currently associated with membrane studies of both plant and animal tissue. In fact the comparison between the properties of plant and animal membranes is an unusual and particularly valuable feature of this book.

The first chapter is concerned with the derivation of well established equations describing the distribution and passage of ions across membranes, including the relationships derived from the general flux equation such as the Goldman expressions. The use of irreversible thermodynamics for theoretical analyses of interactions between membrane fluxes is the subject of the second chapter. Only an elementary introduction is given but it is sufficient to give the reader an insight into the possible applications of this branch of thermodynamics to understanding the nature of solute and water fluxes in biological systems.

In the following chapters the author has attempted, where possible, to use much of the theory given in the earlier part of the book for quantitative analyses of experimental observations both with artificial and biological membranes. Two chapters discuss evidence for active ion transport processes in plant and animal cells and their dependence on cell metabolism. As well as outlining present biochemical knowledge of cation pumps in animal and plant tissue there is some discussion into the possible mechanism for light induced chloride fluxes in plant cells.

Other chapters briefly discuss the electrical characteristics of plant and animal membranes with reference to excitability and correlation of ionic fluxes with measured conductances. There is also a short but useful chapter on the properties of various types of artificial membranes.

Provided this book is used in conjunction with a reasonably detailed lecture course, I would thoroughly recommend it for specialized undergraduate and postgraduate studies. I also think that the author has produced a book which will be particularly valuable as a source of reference for plant and animal physiologists who have research interests in this field of cellular function. Considering the length and nature of this book it is a great pity that the publishers could not produce it in a paperback form at half the present price.

J. Barber

Histones Reviewed

Histones and Nucleohistones. Edited by D. M. P. Phillips. Pp. xii+305. (Plenum: London and New York, 1971.) n.p.

The editor of this recent addition to the very limited number of books devoted to the topic of histones and the enigma of their structure and function in the cell comes from a well known stable in the histone field, although individual chapters are written by authors from several countries. The balance between structure and function is well maintained.

After an introductory chapter on preparation and characterization by E. W. Johns, giving a comprehensive survey of methods with a good coverage of references, we are launched into comparisons of the primary structures of histones and protamines by D. M. P. Phillips. Although this is the smallest chapter it will receive a great deal of attention in view of the current search for an explanation for the dramatic lack of species variation in the primary structures of histones. The author develops the theme of gene duplication to account for homology among histones as has been proposed for the protamines, and leaves one waiting eagerly for further information to become available. One criticism of this chapter is the confusing use of both the older three letter abbreviations for amino-acids and the more recent single letter code—we sometimes get one, sometimes the other and on occasion both, giving unnecessary duplication.

In the third chapter E. M. Bradbury and C. Crane-Robinson give an authoritative critical review of work on the conformation of histones and nucleohistones. This clearly indicates that ideas in this field have not gelled yet, and there is still scope for the brainwave to explain the interrelations between histone and nucleic acid and for the emergence of new techniques.

Unfortunately the authors do not define what they mean by nucleohistone here, for the acidic proteins of the cell nucleus get no mention or part to play. This contrasts with the next chapter by E. Fredericq on the chemical and physical properties of nucleohistones where the acidic proteins present come in for frequent comment in an established portrayal of properties of nucleohistones, collected together for critical appraisal.

It is, however, chiefly for the last two chapters, which constitute a third of the volume, on the functional aspects of chromatin, that the book will be bought and read avidly.

Histone biosynthesis is dealt with by Hnilica, McClure and Spelsberg, first in general terms and then in relation to embryogenesis and the gametes. Very little is left out, and with an up to date list of 282 references the reader feels that he is getting the total picture, including relationships with non-histone proteins.

The final chapter on functional aspects of DNA-associated proteins by Vincent Allfrey provides a lucid summary with 384 references. There are unanswered questions on all sides but this is the nature of the beast and the questions that should be asked become more apparent as the chapter progresses.

A minor irritation in the book is the use of independent chapter references, which entails the happy game of finding the end of the chapter if ever you want to check a reference. But the book is without doubt better than any of the few previous books on histones, giving both a good introduction to the subject and the latest state of the art; it will not become out of date too quickly.

H. J. Cruft

Terpenoids and Steroids

Terpenoids and Steroids. Vol. 1. Senior Reporter K. H. Overton. Pp. xi+557. (The Chemical Society: London, July 1971.) £11.

The aim of this volume is to provide detailed coverage of the literature on terpenoids and steroids from September 1969 to August 1970. It is the first of the

Chemical Society's specialist reports in this field and the authors have therefore included, where necessary, material published in the preceding year. With such a wide range of natural products, within which there are no sharply defined boundaries, it is difficult to decide on the best framework for a report. The procedure adopted takes cognizance of structural relationships, and of the biogenetic paths which provide the basic unifying theme. Part one (terpenoids) thus contains chapters on mono-, sesqui-, di-, tri-, and poly-terpenoids: the last chapter deals with the biosynthesis of both terpenoids and steroids. Part two (steroids) consists of two long "chapters" (the first on properties and reactions, the second on steroid synthesis) which are suitably divided into well chosen smaller sections. The intrinsic importance (biological and pharmacological) of steroids, and their suitability as substrates for mechanistic and spectrometric investigations, is recognized by the almost equal lengths of the two parts of this volume.

The eight authors are to be congratulated on the breadth and depth of their reading. Although exercising discretion in the material reported, they seem to have included all the important developments. Moreover, they have done much more than merely providing a comprehensive list of up to date references for further study: within a reasonably sized volume they have been able to summarize the chief points and to discuss briefly the significance of the publications to which they refer. Even the most active follower of the literature could not have hoped to have kept abreast of so many topics; organic chemists working on any aspect of terpenoids or steroids will find in this admirable volume a most welcome opportunity to see what advances have been made recently in all the related branches of research.

G. D. MEAKINS

Foreign Substances

Foreign Compound Metabolism in Mammals. Vol. 1. Senior Reporter D. E. Hathway. Pp. xvii+455. (The Chemical Society: London, May 1971.) £11.

IN several countries of the world official bodies that formulate regulations concerning the safety in use of drugs, food additives, pesticides and the like now require information about what happens to these chemicals in the animal body, and in the past decade or so there has been a tremendous increase in the output of information on this subject. Much of the older work in this field was covered in the second edition of my book *Detoxication Mechanisms* which appeared in 1959; the volume under review covers the period 1960 to 1969.

This book is the first of a series planned to cover a variety of aspects of the metabolism of foreign compounds and future volumes are to include chapters on special techniques such as whole-body autoradiography and subjects such as drug tolerance and addiction. The six chapters are concerned with: (1), absorption, distribution and excretion; (2), the movement or transference of foreign compounds in the body; (3), the kinetics of drug metabolism; (4), biotransformations — an American term meaning the molecular reactions that compounds undergo in the body; (5), the mechanisms of biotransformations; and (6), species, strain and sex differences in metabolism.

The first three chapters aim to give an introduction to all aspects of the absorption, distribution and excretion of foreign compounds. Such subjects as the permeability of membranes, protein binding, the use of radioactive labels, the various physiological systems of the body and their involvement in drug metabolism, the kinetics of drug metabolism and drug interactions, to mention only a few, are discussed. These chapters are an up to date and readable account of these processes, and can be read with benefit by anybody in and intending to enter the field of biochemical pharmacology and toxicology because they form an important introductory background to the rest of the book. The fourth chapter is by far the largest in the book and covers more than 40 per cent of the pages. It gives a succinct account of the metabolic transformations of selected drugs, food additives, carcinogens, insecticides, herbicides, molluscicides and so forth. It is not claimed to be comprehensive because a coverage of the metabolism of all the compounds studied in the past ten years would require several volumes.

The fifth chapter is a systematic account of the mechanisms of the transformations of foreign compounds in body tissues covering the processes of oxidation, reduction, hydrolysis and conjugation and their enzymatic intricacies. The last chapter deals with three of the many factors which affect the metabolism of foreign compounds; namely, species, strain and sex. Species and strain are factors of considerable importance in the problem of extrapolating results from experimental animals to man. Sex differences in drug metabolism are not important except in rats which, nevertheless, are extensively used in testing.

This book is a useful addition to the literature on the fate of foreign compounds in animals, but unfortunately it does not possess a compound and subject index. The metabolic fates of many chemicals are competently described but to locate a particular compound is tedious.

R. T. WILLIAMS

Intermediary Metabolism

Regulation of Gluconeogenesis. (Ninth Conference of the Gesellschaft für Biologische Chemie.) Edited by Hans-Dieter Söling and Willms Berend. Pp. xii+347. (Georg Thieme: Stuttgart; Academic: New York and London, July 1971.) $12.50; £5.85.

THIS volume is the published result of a similarly entitled conference held in Göttingen in the spring of 1970. As such, it consists of twenty-five invited contributions together with full reports of the informal discussions which followed each principal paper. Even at a first glance it is clear that this book represents something of a turning point in the development of ideas concerning the loci of the rate-limiting steps of gluconeogenesis. To give a single example, it is instructive to note that both glucose 6-phosphatase and fructose 1,6-diphosphatase are conspicuous by their absence, both in the formal and the informal presentations. Even glyceraldehyde 3-phosphate dehydrogenase, a one-time favourite with some workers, has now been forsaken as a possible site of physiological regulation, and there is in evidence a general, although not unanimous, closing of the ranks behind the hypothesis that phosphoenolpyruvate carboxykinase, theoretically always the most likely candidate, is the site of gluconeogenic control. Indeed, much of the text is both directly and indirectly devoted to the consideration of the physiological role of this little understood enzyme and of its neighbour, pyruvate carboxylase.

In any new journal of inconclusive and negative results, the output from gluconeogenesis research groups would perhaps loom largest among the total number of contributions. One must therefore be particularly grateful to the editors and publishers of this volume for the provision of such full coverage of the informal discussion which contains much comment and material that would not normally be considered acceptable for publication by the established scientific journals. Among the problems dissected are: (1), compartmentation phenomena, both intercellular and intracellular; (2), the relationships between pyruvate carboxylase and phosphoenolpyruvate carboxykinase *in vivo* and *in vitro*; (3), gluconeogenesis, or, rather, the lack thereof, in homogenates; (4), the relationships between experimental and physiological situations, particularly with regard to hormone concentrations; (5), the interpretation of metabolite concentrations and crossover data; and (6), the role of the ubiquitous adenosine 3′5′-cyclic monophosphate.

On the debit side, one might perhaps have hoped for some information on, for example, ruminant gluconeogenesis and the role of energetically wasteful cycling; it is also regrettable that the book contains so many not altogether trivial typographical errors and has no index. With these very minor reservations, however, this volume will be warmly welcomed by everybody interested in carbohydrate biochemistry, and not least by final year undergraduate and postgraduate students who may thereby gain some insight into the present problems of intermediary metabolism.

C. I. POGSON

Dog's Life

Behaviour of Wolves, Dogs and Related Canids. By M. W. Fox. Pp. 214. (Jonathan Cape: London, September 1971.) £3.60.

A BOOK of this title is likely to arouse interest among students of animal behaviour and pet-keepers alike; it is probable, however, that the first of these two groups will be disappointed by this volume.

It touches on many problems of social behaviour and organization, and of the evolution of behaviour, and discusses some of the consequences of domestication, all in an easy flowing style. But too often the author is carried away by his writing, and the book leaves the impression of a series of arguments put together in a somewhat haphazard fashion, with many non-sequiturs. For the dog-enthusiast, however, these objections are to some extent compensated for by the presentation of several interesting observations, by the nice illustrations and the excellent layout.

The first chapter, "Evolution and Classification of Canids", provides a detailed discussion on the classification within this family, but little on evolution of behaviour.

In the next chapter the occurrence of various categories of behaviour in different canids is discussed. The comparison of the facial expressions of these carnivores with those of primates is of special interest here, and this is considered in detail. I missed, however, an evaluation of the function of behavioural differences between the canids from an evolutionary point of view. This is indicative of a general shortcoming of the book, which is the lack of reference to ecological studies and behavioural field observations. This shortcoming is irritating especially where the author writes, for example, about the "gradation of sociability from the solitary fox-like species to the more dog-like species". The fact that one can keep several individuals (for example, *Otocyon*) together in a cage does not signify that they are gregarious in their natural environment (*Otocyon* lives in pairs).

The seventh and eighth chapters are probably the best sections of the book, and although they lack any quantitative information, they are interesting because of the author's many years experience in rearing wolves. They deal with development of social relationships and wolves as parents, and it is here that a good background will be found by those interested in the behaviour of domestic dogs. Again, there are fine illustrations.

The tenth chapter, on the comparative ethology of the domestic dog, states differences and similarities between domestic dogs and several other canids, and considers the effects of domestication. There is a long discussion of scent marking and territory, in which the author states ". . . territorial marking, through which one pack (of wolves) or one individual (a red fox) acquires information as to the population density of like-species in a given region". It is one of the many places where the author makes bold statements on a subject which has been extensively discussed by others previously, in a fashion which makes one doubt whether he gave it a great deal of thought.

It would have been useful to have an index, and I was sorry to see the excellent presentation of this book marred by spelling mistakes in almost all the German titles of the list of references. On the whole it is rather an unsatisfactory book to the behaviourist, yet certainly worth the effort of borrowing it from a library.

H. KRUUK

Go to the Ant . . .

William Morton Wheeler, Biologist. By M. A. Evans and H. E. Evans. Pp. xii+363. (Harvard University: Cambridge, Massachusetts; Oxford University: London, July 1971.) £5.25.

THE biography of a scientist who died nearly 35 years ago might either be deemed to be too late to excite interest, or too soon advantageously to rekindle it, but the large number of Wheeler's old students will find it a delight. Others like myself who were influenced directly only by Wheeler's writings will be glad to learn more of the makings of this man, born in 1865 in Milwaukee, whose working life spanned so many of the formative years of American university development and of American science.

Wheeler's early education was at the German–English Academy in Milwaukee, where there flourished a highly cultured community largely of immigrant German stock. He left with a lifelong interest in the classics and in music, a fluency in the German language and a passionate interest in natural history.

When Milwaukee staged an industrial exposition in 1883, an especially attractive exhibit came from Ward's Natural Science Establishment in Rochester, New York. This included a large collection of animals, fossils and casts of fossils. Young Wheeler, still

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Animals of the Arctic

Seven species of phocid seal are found in the Arctic, though their patterns of distribution in the region differ widely. They and all other species of Arctic wildlife are documented and illustrated in *Animals of the Arctic: The Ecology of the Far North* by Bernard Stonehouse. Pp. 172. (Holt, Rinehart and Winston, New York, November 1971.) $10.95.

at the academy, helped Ward set up the exhibits. Soon afterwards he took his first permanent job with Ward in Rochester, where he published a *Catalogue of Specimens of Mollusca and Brachiopoda for Sale at Ward's*, Ward supplying biological material to various universities, schools, museums and private collectors.

Milwaukee decided to found a permanent museum with Ward's special exhibit as a basis and Wheeler returned home to work there, and soon became director. In this new museum his friend and colleague Carl Akeley created the first museum habitat group—a scene of muskrats in a pond. Akeley's later work became a feature in the Field Museum, Chicago, and of the American Museum of Natural History, New York, which set the trend towards realism now followed by many museums.

In the summer of 1889, Wheeler visited the new laboratory at Woods Hole, directed by his former teacher at the German-English Academy in Milwaukee, C. O. Whitman. In this stimulating environment he met biologists such as T. H. Morgan, J. Loeb, E. G. Conklin and H. F. Osborn and many others, and developed a love for marine animals. In 1890 he followed C. O. Whitman to the newly founded Clark University in Worcester (Massachusetts) where he obtained his doctorate for a thesis on the embryology of insects in which he described in detail the embryonic writhings — blastokinesis — which are peculiar to insects with yolky eggs.

By 1892 he was teaching in Chicago and from there he visited Europe, spending some months with Boveri in Würzburg where he used the latest methods of section cutting to study the excretory system of the lamprey. He continued his summer visits to Woods Hole and in 1894 published a detailed study of the curious sex change in the marine worm *Myzostoma*. It was his move to Austin, Texas, in 1899 which brought him into contact with the ants which he studied with such fascination in later years. In 1908 he became professor of economic entomology and later dean at the Bussey Institution in Harvard. These years at the Bussey were the most influential in his life and he stayed there until his retirement in 1934, to die three years later.

Wheeler's teaching at so many new institutions had considerable influence on the development of biology. His books, *Ants* (1910) and *The Social Insects* (1928), were widely read by biologists. These books emphasized that what the animal really did was at least as important as its structure alone; so was born the subject which he termed ethology which has more recently been developed so successfully by Lorenz, Tinbergen and others.

A collection of essays, *Foibles of Insects and Men* (1928), in which his barbed shafts of wit, "liberally suffused with formic acid", aimed largely at "the stuffy and the solemn, not excluding professors of biology", reached the widest circle of readers. Wheeler himself did not rate the value of his scientific contributions in relation to their popularity; he took the greatest pride in his taxonomic work on various groups of flies and on the ants.

Readers of this book will ponder on the contrast between Wheeler's time and ours. Who nowadays could change his job so frequently and work in so many institutions and make such long and profitable trips abroad? Who could now produce important publications in so many biological fields?

Wheeler himself had the gift of clear exposition. His biographers share this ability so that the book can be read, or dipped into, with interest and enjoyment. The book includes twenty-one illustrations of insects and men, a list of Wheeler's 680 publications and an index which will greatly help readers to piece together the strands which make up this book.

G. C. VARLEY

Below the Sea Bed

200,000,000 Years Beneath the Sea. By Peter Briggs. Pp. 228. (Holt, Rinehart and Winston: New York, Chicago and San Francisco, September 1971.) $7.95.

THE author of this book has considerable experience at sea and as a science journalist. The title of his book refers to the oldest sediments recovered by coring deep holes drilled into the ocean floor during the past three years by the very advanced US exploration vessel Ocean Challenger. The book tells chiefly about the ship and the work at sea but the author sets his story against a background of all the evidence and ideas that have led to the new theory of seafloor spreading. It describes how the theory has evolved from topographic, seismic and magnetic studies of the deep ocean floor, particularly of the mid-ocean ridges and their rift valleys in which the continuing upwelling of basalt forms the new ocean floor, and continues with the concept of moving plates of seafloor and continental crustal material now used to explain the great mountain ranges, deep sea trenches, vulcanism and earthquakes. Where they collide, one sinks below the other and where ocean floor moves towards the land as along the west coast of America, seafloor material is subthrusted below the land. Some of the metalliferous provinces and ore concentrations are being explained in these terms, and from the practical as well as scientific point of view study of the sediments and rocks below the sea bed has become exciting and important.

After a general introduction to the history and background geology, the author tells of the now almost legendary American Miscellaneous Society and its drilling committee whose informal and formal discussions and negotiations led to the Mohole Project and to experimental drilling in deep water. The author implies that the successful investigation of the sediments was one of the factors which diverted interest from the more spectacular project of drilling right through the Earth's crust. It established the feasibility of the Deep Sea Drilling Project that followed, and provided much of the necessary design data. The new project is managed by the Scripps Institution, but the ship is run by Global Marine Inc, a sizable commercial oil-drilling concern which achieves real economy by choosing good men and paying and treating them exceptionally well. They work hard and are unquestionably competent and interested in new methods and equipment. The whole ship's company, about seventy in all, is changed at the end of each voyage of about two months and the officers and crew alternate one voyage on and the next on vacation. The decisions are made promptly by the specialists directly concerned, and who best understand the scientists, sailors and work at sea. There is none of the over centralized regulation, and insistence on controlling everything of many government funded projects.

The book describes the day to day successes and difficulties of thirteen voyages, equivalent to well over two trips round the world. The reader gets an impression of about two hundred deep drillings, the longest drill string being more than 4 miles and the deepest sediment penetration 3,231 feet. Drilling was sometimes stopped by a hard layer of flinty rock called chert which wears out the diamond bits after a few feet of drilling, but a method of re-entering the same hole has been worked out and tried successfully at a depth of 2 miles. A bit-changing operation might take 15 hours. More than three hundred US scientists have been concerned in the project and perhaps a tenth of this number have been from abroad. The cost for 4½ years work is to be nearly 35 million dollars.

The author gives a lively impression of how the programmes are planned and executed. He emphasizes the value of invertebrate palaeontology which seemed a very remote sort of science before the days of oil wells, and which now provides key personnel for the work at sea. Geologists and scientists who have worked at sea will probably be the most appreciative and satisfied readers of the book but it can be recommended to anybody with scientific interests.

G. E. R. DEACON

(Continued from page 267)

time and more efficiently lost from the surface. Such a decoupling of the short lived and long lived radioactivities at 4.5 billion yr ago from the outer 200 km of the Moon might be expected to have considerable effect on the Moon's subsequent history. Because of the localized concentrations of ^{40}K in the fescon, local pockets of basaltic liquids associated with fescons would be formed. Impact-triggered eruptions could result in flooding of the regions above the fescons (Fig. 3) with spillage into adjacent areas. The mascons themselves may be primarily a result of near-surface effects associated with mare formation[14,15], but the distribution of circular maria on the lunar surface and the production of basaltic liquids a billion years after the origin of the Moon result from the formation of fescons.

Many workers have noted that the mare basalts show gross depletions of the alkalis, and several chalcophile and siderophile elements relative to chondrites. The depletion of alkali elements has been attributed to volatilization from the Moon[14,21] and to pre-lunar fractionation processes[22,24]. Evidence obtained from Pb-U and Rb-Sr isotopic techniques[4,25] shows that these fractionations have occurred before or during the first few million years of the Moon's history. Strong arguments against volatilization following lunar accretion as an exclusive source of these fractionations have been presented[22]. In our model, the Fe-S liquid segregation will cause a depletion of the chalcophile, siderophile, and alkali elements, in addition to any pre-lunar fractionations.

Following the initial melting 4.6 billion yr ago, the outer regions of the Moon underwent extensive fractional crystallization[9], producing the anorthositic crust by flotation of plagioclase cumulates[15] accompanied by sinking of pyroxene and ilmenite. The net result of this fractional crystallization process would be a mineralogically and chemically zoned outer region of the Moon, grading from Fe, Ti rich material in the lower parts to residual material near the top enriched in trace elements such as K, Ba, rare-earths, U and Th, overlain by an anorthositic crust.

About 1.0–1.5 billion yr later, the heat generated in the fescons by ^{40}K would partially melt the already chemically differentiated outer layer, producing the ferro-basalts of the maria. Thus, the abundances of many trace elements such as Ba, U, Th and the rare earths in these mare basalts would have been controlled both by the enrichments in fractional crystallization in the initial melting and the partial melting about a billion years later. The alkalis, in contrast, would have been depleted in the initial melting because of the Fe-S liquid segregation, but would be somewhat enriched in the later partial melting.

Assuming a uniform thermal gradient from 200 km depth to the surface and a conductivity of 10^{-2} calories/cm s ° C, approximate calculations show that to produce and maintain silicate melting temperatures ($\sim$1,000° C) (at the depth of the Fe-S layer) during the first billion years would require the extraction of $\sim$100 p.p.m. of K from the overlying silicate material into the Fe-S layer. A 5% FeS content in the Moon initially would lead to a K concentration of 0.2% in the Fe-S layer. Estimating the K content of the source regions of the mare basalts at $\sim$200 p.p.m.[26] we obtain an initial abundance of 300 p.p.m. K in the outer parts of the Moon, significantly less than that in ordinary chondrites. An entire Moon of this K content would not undergo melting in the interior regions, as Urey and MacDonald showed[27].

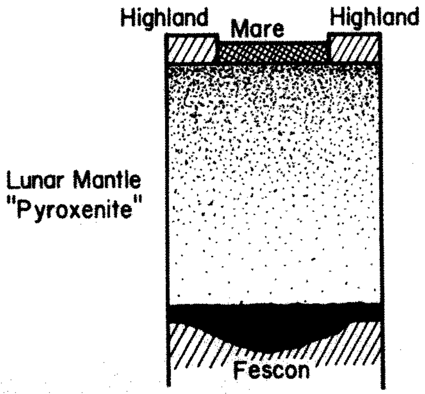

Fig. 3 Fescon and mare 3.0–3.6×10^9 yr ago.

The hypothesis of Fe-S segregation and formation of fescons used in our model of early lunar differentiation can be tested in future lunar missions. Seismic studies bearing on the interior structure of the Moon should in principle detect the Fe-S layer and the fescons. The localized concentration of ^{40}K in the fescons may be reflected by higher heat flow in the circular mare areas and can be verified by heat flow studies.

We suggest that Fe-S segregation plays a major role in the early chemical and physical history not only of the Moon and Earth[20] but of other terrestrial planets as well. Thermal histories of the planets attendant on a possible early segregation of K from U and Th remain to be studied.

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New Prospect for Gamma-Ray-Line Astronomy

THE prospects for gamma-ray-line astronomy associated with the anticipated occurrence of radioactivity in interstellar space have already been outlined[1-4]. Each successive clarification of these possibilities has resulted from major clarifications in the theory of nucleosynthesis, and in this communication I wish to report another step. The supposition that the elements are coproduced in exploding stars has been greatly strengthened by quantitative success[5] in the past few years. A new development within that general picture now suggests that detectable amounts of ^{60}Fe exist in nearby explosive remnants. ^{60}Fe has a half-life $\tau_{1/2} = 3 \times 10^5$ yr, and the subsequent decay of its ^{60}Co daughter is accompanied by a two-gamma-ray cascade with energies $E_\gamma = 1.17$ MeV and 1.33 MeV (ref. 6). This pair of equal-intensity lines is the signature that can identify ^{60}Fe in interstellar space. The other important feature is, of course, its half-life, which is long enough to allow the radioactivity to persist long after (in terms of recorded history) the explosive event.

For discussion I take this very simple model: all solar nuclei were coproduced in 1.7×10^9 explosive events occurring on the average every 3 yr over the first half of the galactic lifetime and now occurring once every 30 yr[7]. This model lowers the present supernova yield by peaking nucleosynthesis early. An elementary calculation shows that each event on the average must yield 0.06 $M_\odot$ of ^{24}Mg from the carbon shells to account for the roughly 1.0×10^8 $M_\odot$ of ^{24}Mg inferred to have been present in the galaxy if it had the solar composition[8] on the average when the Sun formed and if the total galactic mass is 1.8×10^{11} $M_\odot$. Howard *et al.*[9,10] have shown that the explosions of those same carbon shells produce many rare neutron-rich nuclei by subjecting the heavy elements present *ab initio* in the exploding star to the free-nucleon fluxes generated by the explosion of the carbon. Most of the significant radioactive yields at $A = 45$, 47, 49, 50 decay too quickly for gamma-ray astronomy. Although our publications do not tabulate the long-lived ^{60}Fe yield, it can be summarized as follows. A substantial fraction f_{60}(Cr) of the seed chromium nuclei are driven to ^{60}Cr where they stop because of the intense rate of ^{61}Cr (γ,n) ^{60}Cr. The exact fraction is uncertain because of uncertainty in the neutron separation energy from ^{59}Cr, but for this communication I estimate $f_{60}(\mathrm{Cr}) \simeq 0.5$. Because only about 1% of seed nuclei have been through explosive carbon burning events[9,10], it follows that 0.5×10^{-2} of chromium has been converted to ^{60}Fe in exploding stars. By the preceding argument concerning ^{24}Mg, this amounts to 1.0×10^{-5} $M_\odot$ of ^{60}Fe per average explosive event. This is not the source of ^{60}Ni in nature, the yield being inadequate by about two orders of magnitude.

The yield of ^{60}Fe can greatly exceed the estimate above, however, if a substantial portion of the iron seed nuclei can be converted to ^{60}Fe in the explosion. We found earlier[9,10] that the iron nuclei were driven largely to ^{62}Fe, with only about 10^{-2} to 10^{-4} of Fe remaining at ^{60}Fe. Such yields could at most double the ^{60}Fe yield quoted from Cr seed, so I shall take that value, 1.0×10^{-5} of $M_\odot$ ^{60}Fe, as a reasonable lower limit on the average explosive yield. There is quite another consideration, however, to be made from our indication that 10^{-2} of all Fe have been through such events, because 10^{-2} Fe exceeds by a factor of four the abundances of ^{62}Ni and ^{64}Ni, and is roughly half of the ^{60}Ni abundance. We must therefore pay close attention to the question of where this iron seed ends up. Only ^{60}Ni is sufficiently abundant among nuclei having $A \geq 60$ to hide 10^{-2} of the iron abundance. This suggests that a non-negligible fraction of ^{60}Ni may have been synthesized as ^{60}Fe from ^{56}Fe seed in explosive carbon burning. Although the Fe (n,γ) flow reached ^{62}Fe in our exploratory calculations these do not conclusively eliminate the possibility that it is partly arrested at ^{60}Fe. The (γ,n) lifetime of ^{61}Fe at $T_9 = 2.15$ is only 0.05 s[10], much less than the expansion time. To stop much of the flow at ^{60}Fe therefore requires only a somewhat smaller neutron flux than our calculations indicated. It would therefore be reasonable that the average ^{60}Fe yield was sufficient to produce about half of ^{60}Ni, in which case its value would be 1.0×10^{-3} of ^{60}Fe per explosive event. This value is two orders of magnitude greater than the yield expected from Cr seed, and I will regard it for the present discussion as a reasonable upper bound on the ^{60}Fe yield. If the integrated neutron flux is only about 1/3 of the values shown before[10], and if the (n,γ) cross-section of ^{58}Fe is actually quite small[11], say 1/3 of that for ^{56}Fe, then this same explosion will also contribute a significant fraction of the natural ^{58}Fe abundance. This result may be significant in light of the difficulty[12] of synthesizing ^{58}Fe. This detail, though suggestive, need not concern us further here, except that it also suggests that the actual flow did not largely pass ^{60}Fe. It is the ^{60}Fe yield we are seeking.

Because these expectations depend on a situation in which most of ^{62}Ni and ^{64}Ni and part of ^{60}Ni are the results of Fe seed in explosive carbon burning, I should comment on the fact that ^{60}Ni and ^{62}Ni can be synthesized quite satisfactorily[13] in alpha-rich freezeouts following an *e*-process. The normalization of the alpha-rich freezeout to the alpha-depleted freezeout is not well established, although it fell naturally out of the ^{12}C-detonation model[13]. There is at present no convincing argument that the ^{12}C-detonation model is relevant in its fine details. Probably the only abundance requirement of the alpha-rich zones is the necessity to synthesize ^{58}Ni in the freezeout, but this can be accomplished without the associated synthesis of ^{60}Ni and ^{62}Ni. Thus it is quite possible, but it is by no means necessary, to synthesize ^{60}Ni and ^{62}Ni in the *e*-process freezeout. Because of the necessity of converting the Fe seed in explosive carbon burning into some nucleus, and because ^{58}Fe, ^{60}Ni and ^{62}Ni are the only plausible candidates, I prefer the view that ^{62}Ni, and perhaps a large part of ^{60}Ni, were synthesized in explosive carbon burning. The important difference for gamma-ray astronomy is that the ^{60}Ni synthesized in *e*-process freezeouts is synthesized as ^{60}Zn, whereas the ^{60}Ni synthesized in explosive carbon burning is synthesized as ^{60}Fe, the gamma-ray source in question. Thus in summary I take the explosive yield of ^{60}Fe to be $1.0\beta \times 10^{-5}$ $M_\odot$ per explosion, where β is a number near unity if virtually none ($\lesssim 10^{-3}$) of the Fe seed can be arrested at ^{60}Fe in explosive carbon burning and is a number of order 100 if most of the Fe seed is arrested there. Thus $1 < \beta < 100$. Although this involved argument at present lacks numerical precision regarding the size of β, we can easily see that the result may be important for gamma-ray astronomy.

Let the distance in kpc to an explosive galactic remnant of age t be R (kpc). Then the flux of gamma rays having energy E_i at the Earth is

$$F_i = g_i \frac{\lambda N_0 \, \mathrm{e}^{-\lambda t}}{4\pi R^2} \tag{1}$$

where N_0 is the initial number of nuclei having mean lifetime $1/\lambda$ and g_i is the number of gamma rays having energy E_i emitted per decay. For the ^{60}Fe yield estimated earlier we have, taking $g_i = 1$ for the 1.17 MeV and 1.33 MeV lines[6],

$$F_{60} = 1.3\beta \times 10^{-7} \frac{\exp(-t/4.3 \times 10^5 \text{ yr})}{R^2 \text{ (kpc)}} \text{ cm}^{-2}\text{ s}^{-1} \tag{2}$$

To be detectable from balloons a line flux should exceed 2×10^{-3} cm^{-2} s^{-1} (ref. 2) and to be detectable from satellites it should exceed 4×10^{-5} cm^{-2} s^{-1}. Thus if $\beta = 1$ and we discuss only remnants less than 10^5 yr old we find that the remnants are detectable at 8 pc from balloons and 60 pc from satellites; however, if $\beta = 100$ the detectability distances are ten times greater, thereby extending to almost 1 kpc from satellites. That this distance is quite large can be seen from consideri that a circle of 1 kpc radius constitutes about 0.5% area of the galactic disk. At one per 30 yr has 10^4 explosive events in one ^{60}Fe half about fifty of them should be within 1 kpc distance. Thus a satellite could plausibly see many sources (if the angular size of the remnant falls within the field of view) and, if $\beta = 100$, a remnant at 0.1 kpc might even be detectable from a balloon (for example, Sco XR-1 is at roughly such a distance). These arguments suggest that a gamma-ray telescope with good energy resolution near 1 MeV might profitably look at nearby supernova remnants and pulsars.

It is notable that the 1.156 MeV line from the ^{44}Sc decay in remnants could not be resolved from the 1.173 MeV line from the ^{60}Co decay. Clearly the two possibilities will be distinguished by the equal intensity 1.33 MeV line in the ^{60}Co case. For comparison the ^{44}Sc flux[2] is expected to be

$$F_{44} = 2.1 \times 10^{-2} \frac{\exp(-t/68 \text{ yr})}{R^2 \text{ (kpc)}} \text{ cm}^{-2} \text{ s}^{-1} \tag{3}$$

which is five orders of magnitude greater than ^{60}F immediately after the explosion, but decays much more rapidly. After 800 yr the ^{60}Fe flux would exceed the ^{44}Sc flux. Neither flux should be detectable from the Crab nebula, for instance, although if $\beta = 100$ its ^{60}Fe lines might be marginally detectable from a satellite.

I have been discussing these remnants as if they are resolvable in angle. Such may not be the case, of course. A remnant 10^5 yr old may well have a size of order 100 light years, in which case it would subtend a broad angle at a distance of 10^3 light years or closer. The radiation from such a source could appear as a general galactic background. Inasmuch as the average galactic luminosity in either ^{44}Sc or ^{60}Fe lines is expected to be of order 10^{37} erg s^{-1}, we can easily see that the galactic disk should always be visible in these lines. (I assume the disk to be transparent near 1 MeV.) The disk content of ^{60}Fe is at all times equal to the number of atoms produced in the last mean lifetime of ^{60}Fe (about 1.3×10^4 explosive events). A reasonably wide angle telescope (I took a cone of half angle $\pi/4$) viewing toward the galactic centre should then see a constant flux

$$F_{60} \text{ (galactic)} \approx 1.7 \times 10^{-5} \ \beta \text{ cm}^{-2} \text{ s}^{-1} \tag{4}$$

which is marginal for $\beta = 1$, but an enormous signal if $\beta = 100$. By comparison again, the ^{44}Sc flux would be

$$F_{44} \text{ (galactic)} \approx 4.5 \times 10^{-4} \text{ cm}^{-2} \text{ s}^{-1} \tag{5}$$

for a time average of randomly positioned supernova remnants. In reality the mean lifetime of ^{44}Ti (68 yr) means that the galactic background in ^{44}Sc lines will depend on the actual age and locations of those explosive events within the past century. These are, of course, unknown. The ^{56}Co lines[2], which are even more intense, are also even more time-dependent and require observation of a specific event within about 1 yr of the explosion. As such, they constitute a very special case. Nonetheless, equations (4) and (5) suggest to me that a gamma-ray telescope with high energy resolution near 1 MeV could very advantageously observe the galactic centre from a satellite. Both ^{44}Sc and ^{60}Fe may be detectable, and the ratio of intensities at 1.33 and 1.16 MeV will be required to distinguish the two. The scientific benefit of any of these nuclear gamma-ray lines would be enormous—philosophically similar to the solar-neutrino equipment. As such it certainly merits a great effort.

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Remote Sensing of Molecular Pollutants in the Atmosphere by Stimulated Raman Emission

ONE method of measuring atmospheric molecular pollutants at remote locations uses the Raman backscatter from a laser beam: the scattered wavelengths are characteristic of each pollutant, and their intensities give a measure of the respective concentrations[1–3]. But, because of the isotropic nature of the scatter, large telescopes are required to collect even a small fraction of the total scatter, and so the probing distance is small.

Here we propose a different method of using Raman interactions for pollutant determination. When a laser beam propagates through a mixture of gases, the molecules in the beam can provide signal amplification at any of the Raman wavelengths scattered. This phenomenon, the stimulated Raman effect, causes a signal of the proper wavelength propagating collinearly with the laser beam to be amplified proportionally to the concentration of the corresponding type of molecule in the mixture. And all of the amplified signal can be collected by a detector at the far end of the beam.

To calculate the signal gain, consider a volume V of the beam containing $n_L(z)$ laser photons of wavelength λ_L and $n_R(z)$ photons of wavelength λ_R equal to one of the Raman wavelengths of a certain molecular species in the atmosphere at location z along the direction of the beam. They travel in the same direction at the velocity of light c. The number of photons of wavelength λ_R scattered from the laser beam by the ordinary Raman effect per metre is

$$-\left.\frac{\mathrm{d}n_L(z)}{\mathrm{d}z}\right\}_{\substack{\text{ordinary}\\ \text{Raman, R}}} = 8\pi\left(\frac{\mathrm{d}\sigma}{\mathrm{d}\Omega}\right) N(z) n_L(z) \tag{1}$$

where $N(z)$ is the concentration (molecules per unit volume) of the scattering molecules at z, and $(\mathrm{d}\sigma/\mathrm{d}\Omega)$ is their Raman cross section per unit solid angle and per direction of polarization for the λ_L to λ_R process.

These ordinary Raman photons fall into

$$\frac{8\pi V \Delta \nu}{c\lambda_R^2}$$

modes within the Raman line width $\Delta\nu$.

The stimulated Raman emission rate into one mode produced by each Raman photon present in it is equal to the ordinary Raman emission rate into the mode. So:

$$\begin{aligned} \left.\frac{\mathrm{d}n_R(z)}{\mathrm{d}z}\right\}_{\substack{\text{stimulated}\\ \text{Raman}}} &= \left(\frac{8\pi(\mathrm{d}\sigma/\mathrm{d}\Omega) N(z) n_L(z)}{(8\pi/c\lambda_R^2) V \Delta\nu}\right) n_R(z) \\ &= g(z) n_R(z) \end{aligned} \tag{2}$$

where

$$g(z)=\left(\frac{c\lambda_R^2 N(z)\,(\mathrm{d}\sigma/\mathrm{d}\Omega)}{\Delta\nu}\right)\left(\frac{n_L(z)}{V}\right) \qquad (3)$$

is the gain parameter at z. The $n_R(z)$ photons may belong to several modes. At atmospheric pressure, $\Delta\nu$ is mainly determined by the collision frequency[4] $\nu_c = 6.9 \times 10^9$ Hz.

Numerically, for $\lambda_L = 0.7$ μm (ruby laser):

$$g \simeq 2\times 10^{16}\,(\mathrm{d}\sigma/\mathrm{d}\Omega)\,\zeta P_L(\lambda_R/\lambda_L)^2 \qquad (4)$$

where g is the spatial gain in reciprocal metres, $(\mathrm{d}\sigma/\mathrm{d}\Omega)$ is the scattering cross section in M^2, ζ is the molecular concentration in p.p.m., and P_L is the laser power density in W m^{-2}.

For example, for a 100 MW ruby laser pulse with 100 cm^2 cross section propagating over a length $L = 1$ km simultaneously with a Raman signal downshifted in frequency by the 2,330 cm^{-1} vibrational level of N_2, the signal intensity gain is obtained from (4) by using[5] $\mathrm{d}\sigma/\mathrm{d}\Omega = 1.9 \times 10^{-31}$ cm^2: $e^{gL} \cong e^{4.4} = 81$.

The same laser pulse accompanied by a signal downshifted by 1,150 cm^{-1} propagating through 1 kilometre of air containing $\zeta = 1$ p.p.m. of SO_2 with[5] $\mathrm{d}\sigma/\mathrm{d}\Omega = 3 \times 10^{-31}$ cm^2 gives a gain

$$e^{gL} \simeq 1 + gL \simeq 1 + 10^{-5}$$

From a device point of view, the stimulated Raman method presents analogies with resonant absorption techniques based on beam attenuation measurements at allowed molecular transition wavelengths[5]. Instead of the tunable laser capability required by the latter, it involves a Raman signal source which may consist either of another tunable, low-power laser or of a Raman cell located in the primary beam. Both methods give average concentrations over a path and necessitate equipment at two locations.

One advantage of stimulated Raman is the possibility of compensating for spurious scattering effects (turbulence, Rayleigh, and so on, which are larger than either Raman gain or resonant attenuation alone) by using pairs of pulses in fast succession with the same Raman content but with laser photons in one of them only: the difference between Raman photon counts at the detector measures the stimulated emission. Another advantage is the possibility of using resonant Raman[6] which enhances the cross section for the pollutant molecules alone, thus compensating for their typically small concentration compared with N_2 and O_2.

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Explosive or Detonative Phase Transitions on a Geological Scale

IN both the geological and chemical literature[1-6] the possibility has been suggested that rapid polymorphic transitions provide a source mechanism for medium to deep focus earthquakes. The properties, and in particular the sign of the volume change, of "laboratory scale" rapidly phase transforming systems have not previously been considered with a view to providing further information on the proposed geological systems. There are a number of reported cases, some of which[7-17] are listed in Table 1, of transitions from a metastable state to a stable state accompanied by acoustic phenomena or shock waves. The sign of the density change during phase transition may be either positive (for example, crystallization of nickel[8]) or negative (for example, the phase change of explosive antimony[10,11]).

In nature, a phase change may take place in volumes of the order of cubic kilometres. This change would spread through the volume accompanied by a shock wave. In fact for this mechanism to operate, the transition must be induced by the shock wave and the transition itself must add energy to the shock wave. Although the energy per gram is small, because the total mass is large the total energy released might be very large indeed.

Table 1 Rapid Phase Transformations

System	Ref.
Crystallization from supersaturated solution	
Water-sulphite	7
Crystallization from supercooled melt	
Nickel	8
Bismuth	9
Polymorphic transitions	
Antimony	10
Arsenic	12,13
Iron, austenite→martensite	14
Lead azide, β→α	15
Polymerization	
Maleic anhydride	16,17

Modern theories of continental drift and plate tectonics involve the sinking of material at continental margins (see, for example, ref. 18). This may provide the mechanism for the attainment of a metastable state prior to explosive transformation to a denser phase. An explosive transition to a less dense phase is also possible, associated with upward convection[6]. Although the current geophysical view is that earthquake sources are characterized by shear phenomena rather than by solid–solid transitions with volume change[19], the existence of a number of explosive or detonative phase transformations in chemical systems suggests that such a process should not be dismissed as a possible earthquake source mechanism. Indeed, deep focus earthquakes occur at depths up to 700 km in regions (New Zealand, for example) where one might expect, from modern theories of continental drift, the ocean floor to be pushed under a continental plate. At a depth of 700 km the temperature and pressure conditions are such that earthquakes caused by shear phenomena are difficult to imagine, and a mechanism such as the one postulated is required.

Finally, it should be pointed out that these adiabatic processes bear a close relationship to the isenthalpic decompressions suggested by Waldbaum[20] for the volcanism of seismically active zones.

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Plate Consumption: Some Comments from an Island Arc

A COROLLARY of lithospheric plate creation on an Earth of stable radius is that plate is also consumed. The island arcs with their phenomena of intense geophysical disturbance form the logical sinks, and the subduction theory of geosynclines has recently been added to the theory of plate consumption at island arcs.

I offer some comments about the difficulties I have in accepting, in its present form, the "dogma" of plate tectonics and its less well based extension to geosynclinal theory.

An "earthquake occurs when the stresses in some region inside the Earth have accumulated to the point of exceeding the strength of the material in some place, leading rapidly to fracture"[1]. This being so, the absence of earthquakes can be attributed, on the one hand, to absence of appropriate stress or, on the other hand, to either extremely high or extremely low strength of the rock.

In the oceanic plates earthquakes do not occur between the mid-ocean ridge/transform fault systems and the allegedly downgoing part of the plate at some depth to the continental side of a trench[2]. Scholz[3] has supposed "that the deviatoric stresses which are directly responsible for earthquakes must occur quite widely and cannot be restricted to seismic zones" and this has led to his suggestion of variable rock strength based on chemical composition. This does not, however, explain why earthquakes occur in the oceanic plates near the mid-ocean ridges but not again in the plate until that plate is plunging into the mantle, unless major changes in the nature of the oceanic plate occur.

The recent data in support of plate tectonics imply that the sub-ocean mantle–crust system consists of a lithosphere about 100 km thick which behaves mechanically like a rigid (high strength) plate. Press[4] attributes a higher density to this rigid plate than to the mantle beneath it, and presumably the strength of the plate is sufficient to contain the buoyancy forces in this inherently unstable situation. But the paradox of the behaviour of this remarkably rigid plate at the plate boundary must also be recognized[5]. Here the plate plunges into the mantle, bending at angles of between 15° and 90° to do so, and it might be expected that the internal stresses involved would be considerable if the plate is rigid. Yet few earthquakes occur in the oceanic lithosphere beneath a trench[2].

Assumption of an extremely weak sub-oceanic lithosphere, while possibly explaining the lack of earthquakes beneath the ocean floor and at the trench, removes the explanation for earthquakes at the mid-ocean ridge and in the Benioff zone. Further, such a mechanically weak plate could not produce the stress situations behind the island arcs which lead to the greater part of the world's seismicity. The conclusion must be that "the deviatoric stresses directly responsible for earthquakes" do not occur widely.

A negative gravity anomaly is a principal characteristic of the asymmetric active region[6,7]. The coincidence of the negative gravity anomaly and the trench of an active system was widely accepted for many years, but in recent work[6,8] I have stressed that the negative gravity anomalies do not necessarily coincide with the trench but may occur also on the inner side of the trench.

As a development of the plate tectonic hypothesis, it has been suggested that deformed "eugeosynclinal" sediments of the Franciscan type have accreted at plate junctures by subduction[9–11] and that the negative gravity anomalies are the result of the accumulating sediments[10,12]. One of the reasons for linking the negative gravity anomalies with the accumulating sediments is that "the strong negative gravity anomalies . . . are generally displaced towards the island arc"[10]. Thus the pendulum has swung from coincidence of negative gravity anomaly with the trench to the generalization that the anomaly is displaced from the trench.

In fact the axis of negative gravity anomalies may be: (*a*) coincident with or within 20 km of that of the trench (Tonga, Kermadec, Chile); (*b*) displaced towards the inside of the active system by a small distance (Sunda, Japan), or (*c*) displaced quite large distances from the trench (Hikurangi (New Zealand) 200 km, Kamchatka 100 km). While the transport of low density sediments to inconvenient distances under New Zealand and Kamchatka could respond to special pleading, it would appear impossible to explain the gravity anomalies which are coincident with the trench in terms of sediment accretion under the continental slope.

A further point which must be noted is that the amplitudes of the negative gravity anomalies tend to be independent of the rate or direction of relative motion of plates. The greatest negative anomaly is coincident with the Puerto Rico Trench where "the motion is nearly parallel to the strike of the trench"[5].

Whereas the mantle seismicity, volcanism, gravity and heat flow anomalies of island arcs are spatially related in a quite rigorous manner[6,8,13], the position of the trench is not invariant in its geometrical relationship with other features of an island arc[6]. The special problem of the trench is the conflict between the theoretically compressional nature of plate boundaries and the apparently tensional nature of the trench itself. Indeed why the collision of two "rigid" plates should produce a trench is so far unexplained. Such earthquakes as are observed beneath trenches have a fault-plane solution best satisfied by normal faulting[14,15]. A sub-oceanic lithosphere must thus be fracturing and sinking through excess mass rather than by thrusting against its continental neighbour —but then the cause of seismicity and shortening in the continental-side crust is unknown. Elsasser[16] has restated the case for tension at the trenches, a point obscured in many recent discussions, and has pointed out the difficulties in developing a dynamical model for plate consumption.

From a study of the geology and geophysics of geosynclines I concluded that the ultramafic belts, rather than being a product of orogeny, as was then believed, actually predated sedimentation in the geosynclinal pair[17]. This view is now commonly held[18,19]. I also suggested[17] that the Macquarie Ridge was the ultramafic belt of an incipient geosynclinal pair, an idea later developed by the proponents of subduction as a geosynclinal precursor[11]. But these later workers have evolved from the simplicity of plate tectonics a series of "catastrophic" mechanisms of great complexity to explain the emplacement of ultramafic belts[9]. I would like to draw attention once again to the remarkable geophysical and geological similarity between the New Zealand Geosyncline and the Franciscan–Great Valley system[17]. Further, a comparison of Kay's restored Appalachian cross-section[20] with the New Zealand and Californian systems shows that all three are laterally dimensionally equivalent. This indicates that the formation of geosynclines is based on a physico-chemical process rather than catastrophic collision.

Two methods of ultramafic emplacement, the subducted and the obducted, are propounded by the plate tectonicists. There seems, however, to be no independent method of identifying obducted or subducted ultramafics. The Papuan ultramafic belt is quoted[11] as an obducted type and it is alleged that superposed calc-alkaline volcanics are few or absent. But andesitic volcanoes of high potash type are at present active parallel to part of the belt and there are many late Pleistocene to recent volcanic centres north of the ultramafic belt. There is no Benioff zone beneath the andesite volcanoes of Papua, but the conjunction of high potash andesite volcanoes and ultramafics in California, New Zealand and Macquarie Ridge has been noted previously[17] and has led to the suggestion of "mio-geosynclinal" andesites[21] which are in all cases a similar distance from ultramafic belts[13]. The "orogenic" and "mio"-andesites may well be derived by independent processes.

None of the collision models explains the marginal or mio-geosynclines, which everywhere are of similar width (~100 km) and of similar structure. Ernst[22] has given the most serious treatment of the development of the Great Valley sequence, but again it is difficult to envisage the cataclysmic nature of collision tectonics producing such simple and similar structures. A relaxation rather than a perturbation process would seem more appropriate for the formation of mio-geosynclines.

If seafloor spreading is accepted, and there are few dissenters, it is required that either the Earth expand or lithosphere be consumed. There are, however, objections to many of the dynamical implications of presently inferred plate kinematics in the consuming regions. In particular, the concept of subduction as the precursor of a "geosyncline" appears to me untenable and indeed there is grave doubt that geosynclines are the perturbation products of island arcs. The introduction of subducted and obducted ophiolite suites merely reflects this uncertainty.

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BIOLOGICAL SCIENCES

Inhibition of Cyclic 3',5'-AMP Phosphodiesterase in Islet Cells and Other Tissues by Tolbutamide

An explanation of the intracellular mechanism by which sulphonylureas such as tolbutamide and chlorpropamide stimulate the release of insulin from the pancreas[1,2] (as in the treatment of diabetes mellitus) should also account for certain effects of these materials outside the pancreas[3–5]. These include the effect of chlorpropamide in reducing polyuria in patients with diabetes insipidus[4] and the possible involvement of tolbutamide in the increased cardiac mortality of patients treated with the drug[5]. It has been clear for some years that cyclic AMP (cyclic adenosine 3',5'-monophosphate) plays an important part in the regulation of insulin secretion. For example, cyclic AMP causes the release of insulin from pancreas tissue *in vitro*[6]. Further, glucagon increases cyclic AMP activity in islet cells by activating the enzyme adenyl cyclase[7], and theophylline increases cyclic AMP activity by inhibiting phosphodiesterase[8,9]. It is known that the sulphonylureas can influence the activity of cyclic AMP[10,11], and tolbutamide and chlorpropamide inhibit the enzyme phosphodiesterase in the rat kidney[12]. We have now shown that the sulphonylureas may regulate the levels of cyclic AMP not merely in islet cells but in kidney, lung, heart and brain. In particular, the sulphonylureas, like the methylxanthines, inhibit the activity of cyclic AMP phosphodiesterase, which hydrolyses cyclic AMP to 5'-AMP[8,9], which provides a plausible explanation for their effects in the pancreas and elsewhere.

We studied cyclic AMP phosphodiesterase activity in a tolbutamide-sensitive insulin-secreting islet cell tumour of the Syrian golden hamster (*Mesocricetus auratus auratus*)[13], which also contains glucagon-sensitive adenyl cyclase (manuscript in preparation). Tumours, 2–5 cm in diameter, were removed, homogenized in 10 volumes of 0.3 M sucrose with 2 mM $MgCl_2$ and centrifuged at 10,000*g* for 10 min. More than 80% of the phosphodiesterase activity and no detectable 5' nucleotidase activity was in the 10,000*g* supernatant fraction which was brought to 50% saturation with solid ammonium sulphate. The precipitate was then dissolved in 0.1 M Tris HCl (*p*H 7.5) containing 1 mM EDTA, dialysed against this buffer, and stored at −60° C until use.

Phosphodiesterase activity was measured by the hydrolysis of ^{3}H-cyclic AMP. Unless otherwise stated, the incubation mixture contained 0.1 M Tris HCl (*p*H 6.8), 2.5 mM $MgCl_2$, 0.1 mM EDTA, 0.001 mM ^{3}H-cyclic AMP (10,000–20,000 c.m.p.) and 21 μg of islet cell phosphodiesterase, in 0.1 ml. Reactions were begun by the addition of phosphodiesterase. After incubation for 20 min at 37° C, $ZnSO_4$ and $Ba(OH)_2$ were added to stop the reaction and to precipitate the ^{3}H-5'-AMP formed by the action of the phosphodiesterase[14]; the unhydrolysed ^{3}H-cyclic AMP in the supernatant fraction was measured by liquid scintillation. Phosphodiesterase activity was calculated from the decrease in ^{3}H-cyclic AMP. After prolonged treatment with islet cell phosphodiesterase, more than 90% of the radioactivity was precipitated by $ZnSO_4$-$Ba(OH)_2$. Further, in several experiments, the radioactivity remaining in the $ZnSO_4$-$Ba(OH)_2$ supernatant after phosphodiesterase treatment either with or without tolbutamide was identified as ^{3}H-cyclic AMP by chromatography on 'Dowex-50'. We used 10^{-6} M cyclic AMP in the phosphodiesterase assay in order to approximate the intracellular concentration of the nucleotide. The apparent K_m for cyclic AMP of our phosphodiesterase preparation is about 2×10^{-6} M, so that phosphodiesterase activity in these conditions was not strictly linear with time. We therefore studied phosphodiesterase activity only in the range of 0–40% hydrolysis of the ^{3}H-cyclic AMP, within which range the reaction rate was approximately linear with time and with enzyme concentration. Although we studied

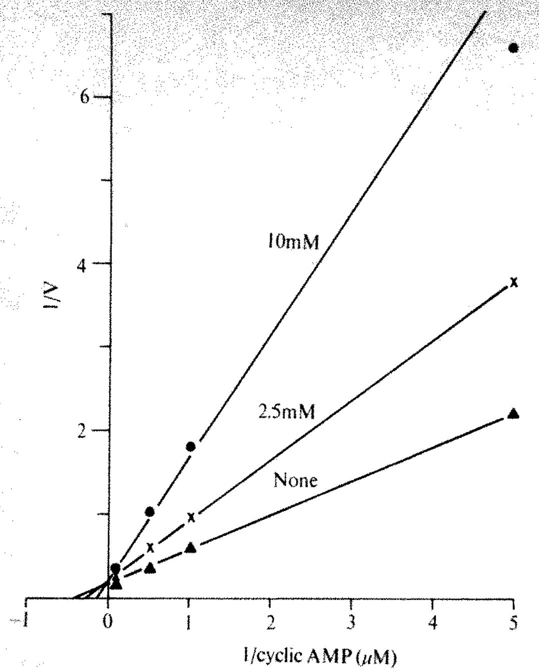

Fig. 1 Effect of tolbutamide concentration on hamster tumour phosphodiesterase activity. The ordinate, 1/V, is the reciprocal of enzyme velocity, expressed as pmol cyclic AMP hydrolysed/min.

phosphodiesterase activity at *p*H 6.8, inhibition was similar at 7.0, 7.5 and 8.0.

Tolbutamide produced substantial inhibition of phosphodiesterase activity (Table 1). Another sulphonylurea, 1-butyl-3-[(*p*-acetyl phenyl) sulphonyl][2] urea, had a similar effect. Both sulphonylureas were slightly less active than the methylxanthines, caffeine and theophylline. This inhibitory action depended on the intact sulphonylurea structure because a mixture of the sulphonic acid and urea moieties of tolbutamide had little inhibitory activity. The inhibition of phosphodiesterase activity by tolbutamide seemed to be competitive (Fig. 1). In several experiments, the K_I was about 3 mM. Although this phosphodiesterase is an Mg^{2+}-dependent enzyme, the inhibition by tolbutamide was independent of Mg^{2+}, for inhibition by 8 mM tolbutamide was identical for the range of 2.5–10 mM $MgCl_2$.

Other studies revealed that tolbutamide inhibited phosphodiesterase activity in preparations of rat brain, liver, lung, and kidney (Table 2). To show more clearly that tolbutamide interacted directly with the phosphodiesterase, purified heart phosphodiesterase (Boehringer) was tested. Tolbutamide also inhibited this purified enzyme, with a K_I similar to that found with the islet cell preparation (3 mM) (not shown).

Inhibition of phosphodiesterase activity by sulphonylureas provides an attractive explanation of their insulinogenic action. Although the plasma concentrations produced by standard oral doses of tolbutamide in man (0.3–0.7 mM)[3,15] cause only slight inhibition of phosphodiesterase activity *in vitro*, nothing is known about the rapidity of uptake or the intracellular concentration of sulphonylureas in β-cells. Also, Beavo *et al.* demonstrated that methylxanthines produce significant lipolysis in adipose tissue at concentrations which cause less than 20% inhibition of phosphodiesterase activity[16]. Further, small doses of theophylline can increase plasma insulin levels in man[8]. But phenothiazines[17], reserpine[17], thiadiazines[18], diazoxide[18], papaverine[19], and triiodothyronine[20] all also inhibit phosphodiesterase activity. The significance *in vivo* of phosphodiesterase inhibition *in vitro* is unclear. Sulphonylureas do not have striking effects in most extra-pancreatic tissues, and so these compounds may not readily enter, or may be rapidly inactivated in, most other tissues. Further, tolbutamide may have actions other than phosphodiesterase inhibition. In contrast to theophylline, tolbutamide inhibits lipolysis in adipose tissue. The ability of tolbutamide to uncouple oxidative phosphorylation has been proposed as the mechanism of its anti-lipolytic action[21]. Studies of the effect of sulphonylureas on tissue cyclic AMP levels will be required to test the hypothesis that these compounds produce significant inhibition of phosphodiesterase activity *in vivo*; such studies are now in progress in our laboratory.

Table 1 Inhibition of Tumour Phosphodiesterase by Methylxanthines and Sulphonylureas

Addition (10 mM)	Phosphodiesterase activity remaining (%)
None	100
Caffeine	18
Theophylline	31
1-Butyl-3-[(*p*-acetyl phenyl) sulphonyl] urea	43
Tolbutamide	47
p-Toluenesulphonic acid + butylurea	85

Hamster tumour phosphodiesterase was assayed in the presence of the compounds listed above; enzyme activity is expressed as the percentage of activity found in the absence of inhibitors.

Table 2 Inhibition of Phosphodiesterase by Tolbutamide in Rat Tissues

Tissue	Protein (μg)	Nmol cyclic AMP hydrolysed/20 min/μg protein: Without tolbutamide	Tolbutamide (5 mM)
Brain	(3)	163	90
Kidney	(7)	83	53
Lung	(6)	71	35
Liver	(4)	22	13

In this experiment 1 g of tissue was homogenized in ten volumes of 0.3 M sucrose with 0.001 M $MgCl_2$ and then centrifuged at 10,000*g* for 10 min. The supernatant was dialysed against 0.1 M Tris (*p*H 7.5) with 0.001 M EDTA for 12 h, then used in the phosphodiesterase assay.

We conclude that sulphonylureas, like methylxanthines, can inhibit cyclic AMP phosphodiesterase activity in many tissues. In kidney, inhibition of phosphodiesterase activity may lead to potentiation of vasopressin action and increased urinary excretion of cyclic AMP[10–12]. Inhibition of phosphodiesterase activity in β-cells may be the mechanism by which sulphonylureas stimulate insulin secretion.

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Note added in proof. Since this manuscript was submitted for publication, the work of Chaudhuri and Wines (*J. Lab. Clin. Med.*, **76**, 863; 1970) has come to our attention. These workers were the first to report that sulphonylureas inhibit cyclic AMP phosphodiesterase.

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Thallium as a Vital Stain for Yeast Mitochondria

BLACK, hexagonal crystals of thallium oxide, $\mathrm{Tl_2O_3}$ (identified by their shape and colour), appear in some cells of some strains of *Saccharomyces cerevisiae* when the culture is grown in nutrient medium containing 125 p.p.m. of thallium sulphate. The black, hexagonal plates of $\mathrm{Tl_2O_3}$ lie in a space between the cell wall and the plasma membrane. Usually only one large crystal is present, but as many as six small ones may appear; all are outside the protoplast. When a crystal is viewed from the edge, a bulge in the cell wall appears right over the crystal. The large crystals bend to conform to the curvature of the cell (Fig. 1).

The cristate mitochondria are not visible in the living yeast cell and are difficult to fix and stain, but Mr Michael Todd, working with Dr Hewson Swift, has established (by an original staining method, personal communication) that a single layer of regularly arranged, cristate mitochondria (almost in contact with each other) lies in contact with the inner surface of the plasma membrane of the yeast cell.

In some of the cells grown in thallium, as many as forty cristate mitochondria are stained black by thallium (Fig. 2). The layer of irregularly elliptical, black-stained, cristate mitochondria lies against the inner layer of the plasma membrane. In some mitochondria only a small black dot of stain appears.

A layer of lipolated mitochondria covers the outer surface of the nuclear membrane and the spindle-reservoir of the yeast cell[1]. The lipolated mitochondria darkened by refraction can easily be distinguished from the jet-black, thallium-stained, cristate mitochondria (Fig. 2). The lipolated mitochondria do not take up thallium.

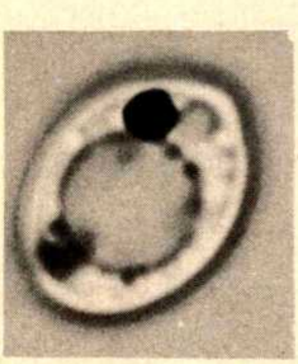

Fig. 1 A yeast cell containing two flat, black, hexagonal crystals of thallium oxide fitted between the cell wall and the plasma membrane. Only one crystal is in focus. Lipolated mitochondria darkened by refraction and others that are bright and refractile lie on the surface of the nuclear vacuole.

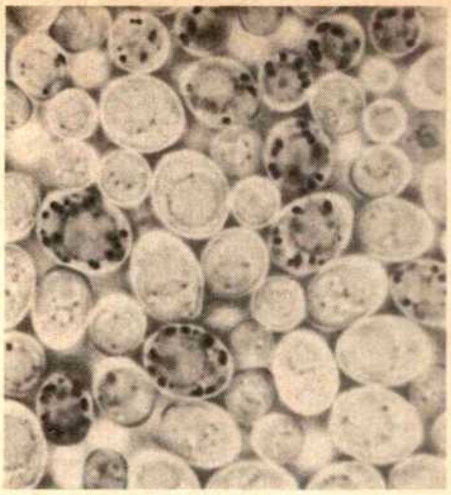

Fig. 2 A culture in which some cells contain a single layer of thallium-stained, cristate mitochondria lying against the inner wall of the plasma membrane.

When cells grown in thallium are spread on nutrient agar, the unaffected cells bud rapidly and produce colonies.

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Unique High Affinity Uptake Systems for Glycine, Glutamic and Aspartic Acids in Central Nervous Tissue of the Rat

NEUROPHYSIOLOGICAL experiments suggest that several amino-acids, especially glycine and glutamic, aspartic and gamma-aminobutyric (GABA) acids, are neurotransmitters in the central nervous system[1–3]. But careful subcellular[4,5] and regional studies[6–8] have not provided supporting neurochemical evidence, because amino-acids, with the possible exception of GABA, also have general metabolic functions in nervous tissue.

Biochemical studies of transmitters in the central nervous system have been facilitated by the discovery of specific uptake systems into neurones with selective high affinities for various putative transmitters[9–14]. There is evidence that such re-uptake mechanisms peripherally inactivate synaptically released catecholamines[9] and it has been postulated that they account for the synaptic inactivation of other neurotransmitters. If amino-acids are neurotransmitters, they might be accumulated into neurones by similar selective uptake. Transport systems have been described for amino-acids in brain tissue, which, however, have relatively low affinity[15]. For this reason and because these transport systems exist for all amino-acids in numerous tissues outside the central nervous system, it is not likely that they have a specific function in inactivating postulated "neurotransmitter pools" of certain amino-acids. Uptake systems for hypothetical "transmitter pools" of amino-acids might be anticipated to have more affinity for their substrates than do general amino-

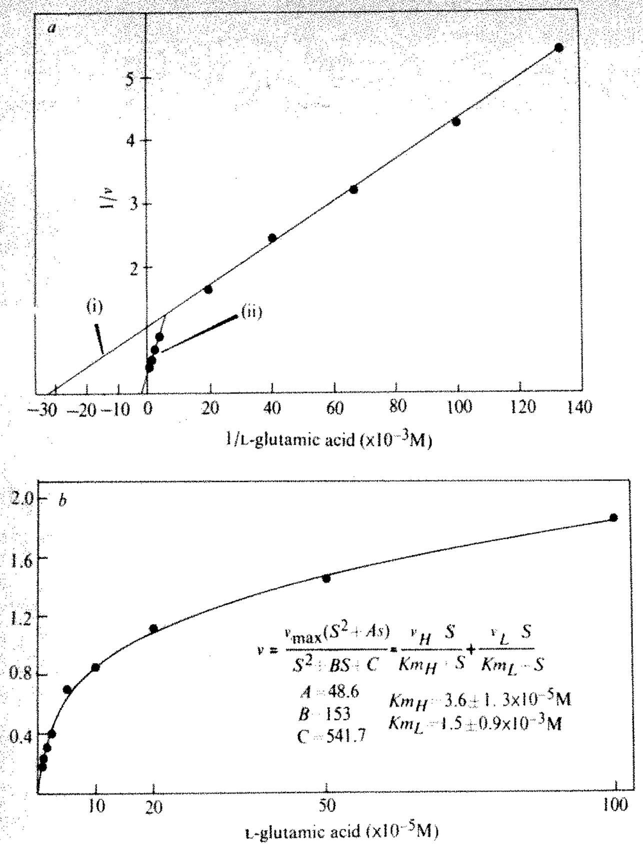

Fig. 1 *a*, Double-reciprocal plot of velocity (*v*) of L-glutamic acid accumulation into homogenates of rat cerebral cortex at different concentrations. Each point is the mean of four determinations. Velocity is expressed as μmol of L-glutamic acid/g/4 min. (i) High affinity system ($Km_H = 3.6 \pm 1.3 \times 10^{-5}$ M); (ii) low affinity system ($Km_L = 1.5 \pm 0.9 \times 10^{-3}$ M). *b*, Computed least squares fit of the same velocity of L-glutamic acid uptake data as in *a*, assuming transport by a two component system. Analysis of these data assuming a one component system gave a poor fit.

acid transports. Demonstration of such high affinity transport systems for physiologically active amino-acids would provide neurochemical support for their transmitter function.

We have examined the accumulation of several amino-acids into synaptosomes (pinched off nerve terminals) of rat cerebral cortex and spinal cord. All of them were accumulated by low affinity saturable mechanisms as in brain slices[15]. In addition, L-glutamic and L-aspartic acids in the cerebral cortex and spinal cord and glycine in the spinal cord had unique high affinity uptake systems.

Male Sprague–Dawley rats (150–200 g) were decapitated; the cerebral cortex or lumbosacral spinal cord were rapidly dissected and homogenized in 20 volumes of ice-cold 0.32 M sucrose in a Potter–Elvehjem glass homogenizer fitted with a 'Teflon' pestle (0.004–0.006 inch clearance). After centrifugation at 1,000*g* for 10 min, the pellet was discarded and a 0.2 ml. aliquot of the supernatant fluid was added to 3.8 ml. of Krebs–Henseleit bicarbonate solution with 11.1 mM glucose, containing varying concentrations of radiolabelled L-amino-acids and agitated at 37° C under O_2–CO_2 (95 : 5) for 4 min. After the incubation mixture had been centrifuged at 27,000*g* for 15 min, radioactivity in the supernatant fluid was assayed. The pellets were washed with ice-cold 0.9% NaCl, recentrifuged at 48,000*g* for 10 min at 4° C and accumulated radioactivity was extracted into 'Triton X-100': toluene phosphor and assayed by liquid scintillation spectrometry. Paper chromatographic analysis in three systems revealed that for all amino-acids examined, more than 90% of the radioactivity in the pellets was unmetabolized. Essentially no radioactivity remained in perchloric acid precipitates of the pellets, suggesting negligible incorporation of the amino-acids into protein under these conditions. The accumulation of radioactivity was linear for at least 4 min and with varying concentrations of tissue homogenates.

When pellets obtained from these incubations were layered on continuous sucrose density gradients (0.32–1.5 M) and centrifuged for 90 min[10], the accumulated amino-acids were localized to an area of the gradient enriched in synaptosomes[10] and separable from the profile of monoamine oxidase activity, a mitochondrial marker. Hypotonic shock completely liberated the particulate amino-acids. These observations indicated that the ^{3}H-amino-acids were accumulated predominantly by synaptosomes.

^{3}H-L-amino-acids (specific activity 1–5 Ci/mmol) were obtained from the New England Nuclear Corporation. The accumulation of amino-acids was examined with 6–10 concentrations of amino-acids ranging from 10^{-8} to 2×10^{-3} M. Kinetics of uptake were determined by double-reciprocal plots[16] and by least squares fitting of a substrate–velocity curve to the data with computer programs donated by W. W. Cleland which provided *Km* values and their standard errors[17].

In the cerebral cortex, double reciprocal plots for alanine, arginine, leucine, serine and glycine described straight lines with positive ordinate intercepts. Single transport system curves gave the best fit for these results, with *Km* values of 0.2–0.8 × 10^{-3} M (Table 1). Double reciprocal plots for the accumulation of glutamic and aspartic acids, however, produced curves (Fig. 1*a* and *b*) which could be resolved into two components graphically as well as by computer analysis with calculated *Km* values of 2–3×10^{-5} M and about 0.4–1.5×10^{-3} M for the high and low affinity uptake systems respectively. We found a similar dual affinity uptake system for L-glutamic acid in rat cerebral cortical slices.

In the spinal cord, double reciprocal plots for the accumulation of alanine, arginine, leucine and serine yielded single straight lines with *Km* values of 1–9×10^{-3} M. Those for glutamic and aspartic acids and glycine, however, described curves that could be resolved into two components. The high affinity transports for these three amino-acids had *Km* values of about 2×10^{-5} M, while the low affinity uptake *Km* values were about 4×10^{-3} M, 2×10^{-3} M, and 1×10^{-3} M for aspartic acid, glutamic acid and glycine respectively (Table 1).

Glutamic and aspartic acids are similar chemically and their uptake in cerebral cortex and spinal cord is kinetically similar, and so they may be accumulated by the same transport system. We therefore assessed the mutual inhibition of glutamic and aspartic acid uptake by two kinetic techniques. In the Lineweaver–Burk technique[16] varying amounts of one^3 H-L-amino-acid were incubated with a fixed amount of the other unlabelled amino-acid, while in the method of Dixon[18] two

Table 1 Kinetics of Amino-acid Uptake into Homogenates of Rat Central Nervous System

Amino-acid	*Km* values × 10^{-4} M Low affinity uptake	High affinity uptake
Cerebral cortex		
L-Aspartic acid	3.68 ± 1.94	0.169 ± 0.128
L-Glutamic acid	14.97 ± 9.59	0.362 ± 0.129
Glycine	7.63 ± 0.53	—
L-Alanine	4.53 ± 0.24	—
L-Arginine	6.24 ± 1.11	—
L-Leucine	3.51 ± 0.47	—
L-Serine	2.16 ± 0.35	—
Spinal cord		
L-Aspartic acid	37.62 ± 14.17	0.215 ± 0.077
L-Glutamic acid	16.73 ± 6.48	0.189 ± 0.058
Glycine	9.23 ± 6.38	0.265 ± 0.141
L-Alanine	10.58 ± 0.71	—
L-Arginine	26.79 ± 7.58	—
L-Leucine	91.36 ± 30.18	—
L-Serine	10.81 ± 2.06	—

Km values and their standard errors were determined as described in the text. A minimum of six concentrations of every amino-acid were incubated in quadruplicate with homogenates.

concentrations of the labelled amino-acid were used with varying concentrations of the other unlabelled amino-acid. In both cerebral cortex and spinal cord, mutual inhibition of glutamic and aspartic acid uptake was competitive. With both techniques, the *Ki* value for inhibition of ^{3}H-glutamic acid uptake in the cerebral cortex and spinal cord by aspartic acid was 3×10^{-5} M. The *Ki* values for inhibition of ^{3}H-aspartic acid accumulation by glutamic acid in cerebral cortex and spinal cord were 3.5×10^{-5} M and 4.0×10^{-5} M respectively. The competitive mutual inhibition of the uptake of glutamic and aspartic acids and the similarity of *Ki* and *Km* values indicate that these two amino-acids can share the same transport system.

The active uptake of GABA, a metabolite of glutamic acid, into brain slices has a *Km* value of about 3×10^{-5} M[14]. GABA concentrations as high as 10^{-3} M, however, failed to reduce synaptosomal ^{3}H-glutamic acid uptake, indicating that neither the low nor high affinity glutamic acid transports involve GABA neurones.

Our results show that representatives of large and small neutral and basic amino-acids are accumulated by synaptosomes in the cerebral cortex and spinal cord by mechanisms resembling their uptake in rat brain slices[11] and other tissues. Glutamic and aspartic acids and glycine utilize, in addition, unique high affinity uptake systems in synaptosomes and brain slices. Hammerschlag, Potter and Vinci independently reported a similar uptake of glutamic acid in rat spinal cord slices[19]. Interestingly, glutamic and aspartic acids, which are neurophysiologically active both in cerebral cortex and spinal cord, showed high affinity uptake systems in both of these regions. Recently, we described a unique population of synaptosomes in the cerebral cortex which selectively accumulate glutamic and aspartic acids, conceivably by the unique uptake system described here[20].

Glycine, which mimics the behaviour of the natural inhibitory transmitter in the spinal cord but not in the cerebral cortex[21], in this study was transported by a high affinity uptake system in the spinal cord but not in the cerebral cortex. Earlier, Neal and Pickles[22] described a high affinity uptake of glycine in rat spinal cord slices, and Johnston and Iversen[23] have independently observed a high affinity transport of glycine in slices and homogenates of rat spinal cord and medulla oblongata but not in the cerebral cortex.

The unique high affinity uptake systems for glutamic and aspartic acids and glycine in central nervous tissue constitute neurochemical evidence that these compounds are transmitter substances. Such uptake systems may terminate their postulated synaptic effects. The occurrence of selective neuronal uptake systems for most putative neurotransmitters, with the possible exception of acetylcholine, suggests that neuronal re-uptake may be a major mechanism for terminating the synaptic activities of neurotransmitters.

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Differential Chromatographic Study of Macromolecular Changes governed by Environmental Factors

GILBERT[1] developed a differential gel chromatographic technique to compare the extents of association of two different haemoglobin species. This entailed the layering of a relatively large volume of solution of one species onto a column equilibrated with an identical concentration of the other. Differences in the weight-average elution volumes of the two solutes resulted in a change of protein concentration at the junction of the two solutions, this effect being a consequence of mass conservation. We wish to explore Gilbert's suggestion[1] that the differential method could be adapted to study the effects of environmental factors (*p*H and ionic strength, I) on the state of a single solute system. The acid expansion of bovine serum albumin provides an example where a variation in *p*H induces a change in conformation and thus in elution volume. The effect of ionic strength on the extent of association of β-lactoglobulin A has also been studied, the change of weight-average elution volume in this instance being used to compare the association constants pertinent to two environments of different ionic strength.

To a 1.8×19.6 cm column of 'Sephadex G-100', thermostated at 20° C and equilibrated with 0.1 I buffer, *p*H 2 (0.01 M HCl, 0.09 M NaCl) was added 60 ml. of bovine serum albumin (0.94 mg/ml.) dissolved in 0.1 I buffer, *p*H 4.6 (0.01 M sodium acetate, 0.01 M acetic acid, 0.09 M NaCl). The eluate from the column was monitored spectrophotometrically at 280 nm and the volume of fractions was determined accurately by weight. The same method was used to obtain the elution profile in an experiment wherein 35.1 ml. of β-lactoglobulin A (9.81 mg/ml.) in 0.1 I buffer, *p*H 4.65 (0.1 M sodium acetate, 0.09 M acetic acid) was applied to a 1.3×23.8 cm column of 'Sephadex G-75', thermostated at 4° C and equilibrated with 0.5 I buffer of the same *p*H (0.1 M sodium acetate, 0.09 M acetic acid, 0.4 M NaCl).

The results obtained in the experiment with bovine serum albumin are shown in Fig. 1*a* from which it is evident that the profile of protein concentration (———) has two distinct plateau regions, the initial elution of protein being at a con-

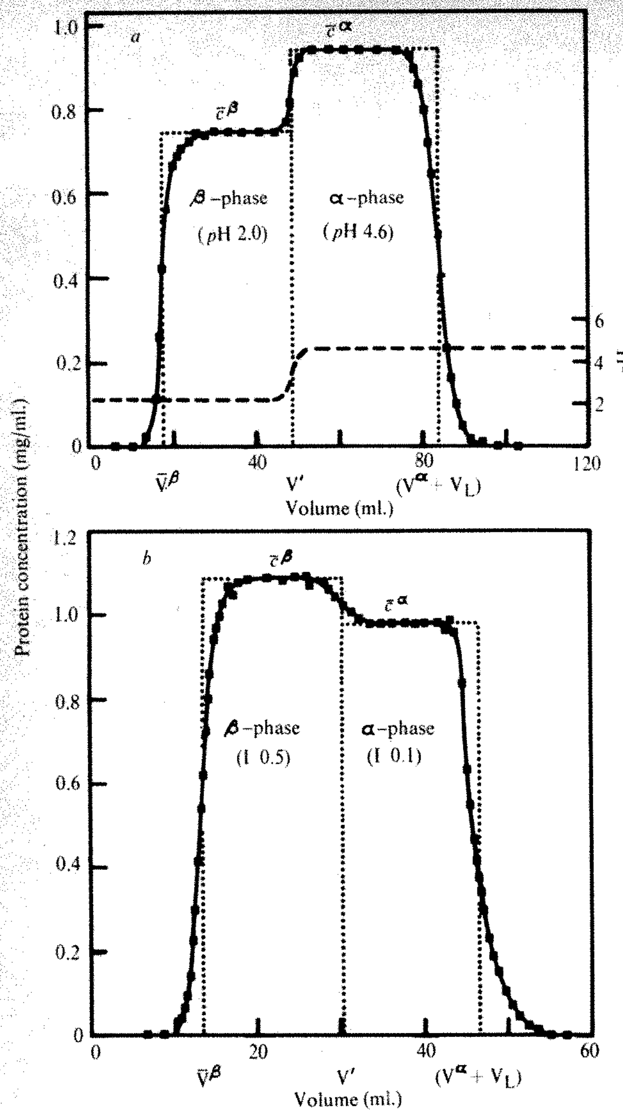

Fig. 1 Elution profiles resulting from (*a*) application of 60 ml. of bovine serum albumin (0.94 mg/ml.) in acetate-chloride buffer (*p*H 4.6) to a 50-ml. column of 'Sephadex G-100' equilibrated with *p*H 2 buffer, and (*b*) application of 35.1 ml. of β-lactoglobulin A (9.81 mg/ml.) in 0.1 I acetate (*p*H 4.65) to a 30-ml. column of 'Sephadex G-75' equilibrated with 0.5 I acetate-chloride buffer (*p*H 4.65). Temperature: *a*, 20° C; *b*, 4° C. Flow rate of each column: 30 ml./h.

centration less than that applied ($\bar{c}^{\alpha}$). The concentration gradient separating the two plateaux coincides with the elution of the proton gradient measured separately and shown by the broken line in Fig. 1*a* (relevant ordinate scale on right). It is noted that the experimental procedure differs from that used by Gilbert[1] inasmuch that prior equilibration of the column with protein is not required: in the present design, the plateau of protein in the *p*H 2 medium is created during the experiment, because of its faster migration rate compared with that of the hydrogen ions. The difference between the two observed plateau concentrations reflects the faster migration rate (smaller elution volume) of bovine serum albumin in the more acidic environment where unfolding has occurred[2]. In the experiment conducted with β-lactoglobulin A (Fig. 1*b*) two plateaux are also observed, but in this case the initial plateau exceeds the applied concentration. This implies that the protein acquires a smaller velocity (larger weight-average elution volume) on passing through the junction between the environments of different ionic strength. Both results are consistent with the following geometric interpretation. The dotted lines in Fig. 1 are median bisectors of observed concentration gradients and permit representation of irregular outlines as rectangles of equivalent area. The total amount of solute added to the column is $\bar{c}^{\alpha} V_L$, where V_L is the loading volume, and for mass to be conserved equals the sum of the areas of the rectangles shown in Fig. 1. Thus

$$\bar{c}^{\alpha} V_L = (V' - \bar{V}^{\beta})\bar{c}^{\beta} + (\bar{V}^{\alpha} + V_L - V')\bar{c}^{\alpha} \qquad (1)$$

which on rearrangement yields

$$\frac{\bar{c}^{\alpha}}{\bar{c}^{\beta}} = \frac{V' - \bar{V}^{\beta}}{V' - \bar{V}^{\alpha}} \qquad (2)$$

where bar superscripts denote constituent quantities[3]. Equation (2) is the Johnston-Ogston equation[4], with V' identified as the elution volume of the median bisector of the protein constituent gradient[5].

In relation to Fig. 1*a*, the following values of the parameters in equation (2) pertain: $\bar{c}^{\alpha} = 0.94$ mg/ml., $V' = 48.8$ ml., $\bar{V}^{\beta} = 17.7$ ml., $\bar{V}^{\alpha} = 24.0$ ml. Their substitution in equation (2) yields a value of 0.75 mg/ml. for $\bar{c}^{\beta}$, in complete agreement with that observed experimentally. In a reverse situation where the column was equilibrated with *p*H 4.6 buffer and bovine serum albumin loaded in a *p*H 2 environment, the condition $\bar{V}^{\alpha} < \bar{V}^{\beta}$ pertained and it was observed that $\bar{c}^{\beta} > \bar{c}^{\alpha}$, the result again being in quantitative accord with equation (2). In connexion with the result obtained with β-lactoglobulin A, summarized in Fig. 1*b*, excellent agreement was again found between observed elution volumes (estimated by first moment calculations[6]) and those predicted on the basis of equation (2), the values being $\bar{V}^{\beta} = 13.5$ ml. and $\bar{V}^{\alpha} = 11.5$ ml. In *p*H 4.65, 0.1 I buffer at 4° C, β-lactoglobulin A seems to exist in solution as an equilibrium mixture of essentially monomer, A (molecular weight 36,000), and tetramer, C (molecular weight 144,000), characterized by an association constant, *K*, of 1.08×10^{-2} $1.^3$ g^{-3} (compare ref. 7, which cites earlier references). The definitions of the equilibrium constant and weight-average elution volume yield the following simultaneous equations.

$$K(c_A^{\alpha})^4 + c_A^{\alpha} - \bar{c}^{\alpha} = 0 \qquad (3)$$

$$\bar{V}^{\alpha}\bar{c}^{\alpha} = V_A c_A^{\alpha} + V_C(\bar{c}^{\alpha} - c_A^{\alpha}) \qquad (4)$$

where c_A^{α} is the equilibrium concentration of monomer in the α-phase and V_A and V_C are the elution volumes of the monomer and tetramer species, respectively. With V_C taken as the void volume of the column (9.3 ml.), equations (3) and (4) were solved for the remaining unknown, $V_A = 13.9$ ml. Equations (3) and (4) may be written for the β-phase, whereupon c_A^{β} and *K* for the 0.5 I environment may be calculated, provided it is assumed that the individual values of V_A and V_C pertain to both α and β phases. A value of 1.0×10^{-4} $1.^3$ g^{-3} was found for *K* in the 0.5 I medium, which clearly shows that an increase of ionic strength promotes the dissociation of tetrameric β-lactoglobulin A.

In summary, the two systems studied illustrate the potential of the differential method for detecting changes in the shape or extent of association of a single solute consequent upon a suitable change of environment. The major advantage of the method is that the change is detected not only by the difference between the observed elution volumes in the two environments ($\bar{V}^{\alpha}$ and $\bar{V}^{\beta}$), but also by the existence of two plateau regions separated by a concentration gradient, the direction of which specifies immediately the relative magnitudes of $\bar{V}^{\alpha}$ and $\bar{V}^{\beta}$. The method should be of particular value for the study, in a wide range of environments, of polymerizing systems which have been previously characterized by a variety of methods under one set of environmental conditions.

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NAD in the Metabolism of Motile Spermatozoa

THE difficulty in attempting to correlate the levels of nicotinamide nucleotide coenzymes with the metabolism of intact animal cells is to distinguish clearly between changes in the coenzyme oxidation-reduction levels which arise from the metabolism of "resting" cells and changes which are associated with other types of cellular activity, such as growth, division and multiplication. Other problems are how to maintain cell viability and what parameters to use in assessing that viability. Spermatozoa are therefore particularly convenient as experimental objects, for they neither grow nor multiply, but can survive for a long time inside and outside the body. Their viability can be checked by quantitative measurements of motility. Furthermore, at least in respect of carbohydrate metabolism, mammalian spermatozoa depend for their supply of energy on extracellular sources, chiefly in the form of fructose which they utilize anaerobically and aerobically, at a rate which is directly and closely related to the degree of sperm motility[1–3]. Thus, changes in the concentration of intracellular coenzymes during fructolysis are directly attributable to carbohydrate metabolism.

The chief end-product of fructolysis in semen is lactic acid, but there are also small amounts of other carbohydrate metabolites, including sorbitol which is oxidized by the intracellular sorbitol dehydrogenase (ketose reductase, L-iditol : NAD oxidoreductase) of spermatozoa[4], according to the equation

$$\text{sorbitol} + \text{NAD}^+ \rightleftharpoons \text{fructose} + \text{NADH} + \text{H}^+$$

The chemical equilibrium of the reaction catalysed by the purified sorbitol dehydrogenase *in vitro* favours the reduction of fructose to sorbitol rather than the reverse, yet in washed but intact and motile ram spermatozoa the added sorbitol is oxidized faster than fructose is reduced. This has been attributed to the ratio of NAD$^+$ to NADH in intact spermatozoa.

We have therefore determined (i) the steady state levels of the oxidized and reduced NAD within spermatozoa and (ii) the direction of changes in the levels of total intracellular NAD$^+$ and NADH within actively metabolizing sperm cells, under the influence of various extracellular substrates. Our procedure for NAD$^+$ and NADH determination is based on that of Greenbaum *et al.*[5], which involves measuring the rate of oxygen uptake with an oxygen electrode with the extracted NAD$^+$ and NADH as rate limiting carriers for hydrogen transfer reactions catalysed by alcohol dehydrogenase, and phenazine methosulphate as electron acceptor.

Washed sperm suspensions were prepared from ram or boar semen by washing and resuspending spermatozoa in Ringer-phosphate[3], and making up to a final concentration of 0.5–2×10^9 sperm/ml. The changes in the concentration of total intracellular NAD$^+$ and NADH, resulting from the addition of various substrates to sperm suspensions, were determined after incubation for 1–60 min, anaerobically, at 25° C.

The results of coenzyme determinations in ram and boar semen (the latter collected as the sperm-rich fraction) and in washed sperm suspensions are shown in Table 1. Our values for the sum of NAD$^+$ and NADH in ram sperm were not very different from those reported by Bistocchi *et al.*[6] for bull epididymal spermatozoa. In boar spermatozoa we found less than half the amount of NAD$^+$+NADH than is present in ram sperm. In both species the values for NAD$^+$ were similar to those recently reported by Brooks[7]. Washing or incubating the washed spermatozoa produced no significant change in the sum of intracellular NAD$^+$ and NADH, but the ratio between the oxidized and reduced form of the coenzyme was significantly altered by the washing procedure; in the ram sperm it declined ($P<0.001$), while in boar sperm it increased ($P<0.05$).

We next investigated exogenous substances for ability to induce changes in the NAD$^+$/NADH ratio in incubated spermatozoa, particularly those metabolites which were known to be readily metabolized by living spermatozoa and are known, from experiments on purified, reconstituted enzyme–coenzyme systems, to require soluble, NAD-linked dehydrogenases for their oxidation or reduction *in vitro*. All substances which changed the oxidation state of NAD in the living sperm cells were identical to those known from enzymological studies to depend on the availability of NAD$^+$ or NADH for oxido-reductions and energy generation. Up to a point, we could predict from the sperm coenzyme response whether or not the sperm cells possess a dehydrogenase capable of reacting with a particular substance. For example, in washed ram spermatozoa the addition of sorbitol produced within 1 min a reduction of sperm-NAD$^+$ to NADH, whereas only a slight reduction occurred when boar spermatozoa were used instead, even on extended incubation. This suggested that boar spermatozoa are deficient in sorbitol dehydrogenase. When we tried to extract the soluble NAD-linked sorbitol dehydrogenase from ram and boar spermatozoa[8], we obtained a highly active preparation from ram spermatozoa, but were unable to detect the enzyme in boar sperm extracts. Similarly, we could show that of the two isomers of lactic acid, only L(+), but not D(−) lactate, can influence the oxidation-reduction state of NAD within spermatozoa, in accordance with what is known about the response of spermatozoa to lactic acid[9,10], and the selective specificity of lactate dehydro-

Table 1 Oxidized and Reduced Forms of NAD in Semen and Washed Suspensions of Motile Spermatozoa

		Number of samples	NAD$^+$	NADH	NAD$^+$+NADH	$\frac{\text{NAD}^+}{(\text{NAD}^+ + \text{NADH})}\times 100$
Ram	Semen	7	19.1 (0.7)	5.5 (0.3)	24.6 (0.8)	77.6 (1.8)
	Washed sperm	9	14.7 (0.8)	9.3 (0.6)	24.0 (1.2)	61.2 (1.3)
Boar	Semen	6	7.5 (1.0)	1.4 (0.4)	9.0 (0.9)	83.5 (5.3)
	Washed sperm	6	9.2 (1.2)	0.3 (0.1)	9.4 (1.2)	96.6 (0.9)

Results are expressed in nmol/10^9 sperm; standard error of the mean in parentheses.

genase for the L(+) isomer. As could be predicted from the nature of the reaction catalysed by lactate dehydrogenase (L-lactate : NAD oxidoreductase)

$$\text{lactate} + \text{NAD}^+ \rightleftharpoons \text{pyruvate} + \text{NADH} + \text{H}^+$$

the addition of lactate to washed suspensions of either ram or boar spermatozoa produced a rapid conversion of NAD⁺ to NADH within the sperm cells, while pyruvate produced the opposite effect. The effect of lactate and pyruvate on the oxidation state of NAD in washed ram spermatozoa is illustrated in Fig. 1, which also includes the result obtained with fructose. The addition of fructose to washed ram spermatozoa produced a small increase in the percentage of NAD⁺, probably because of a small initial reduction of fructose to sorbitol by ram sperm sorbitol dehydrogenase. When this experiment was repeated with washed boar spermatozoa which, as stated above, are deficient in sorbitol dehydrogenase, the effect of added fructose was that of an immediate decrease in the percentage of NAD⁺.

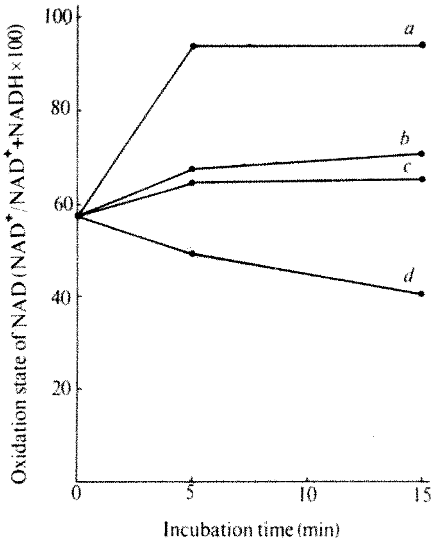

Fig. 1 Effect of fructose, lactate and pyruvate on the oxidation state of NAD in washed ram spermatozoa. The mixtures contained 1.7×10^9 sperm and 2 mg substrate/1 ml., and were incubated at 25° C. *a*, Pyruvate; *b*, fructose; *c*, no addition; *d*, lactate.

Among other exogenous substrates which we have tested, three deserve special mention because of their strong oxidizing influence on sperm-NADH, namely, dihydroxyacetone, oxaloacetic acid and acetoacetic acid. All three substances are known, from previous studies of sperm metabolism, to be metabolized efficiently by motile spermatozoa[3,11].

The influence of nicotinamide nucleotide coenzymes on cell metabolism is well documented[12]. The observations reported here, however, provide insight into the controlling influence of extracellular metabolites on the oxidation-reduction state of NAD within the cells. In motile, actively metabolizing spermatozoa, the ratio between total NAD⁺ and total NADH is regulated in a rapid and highly sensitive manner by energy yielding processes originating in the extracellular environment. Our findings also underline the important role allotted to exogenous substrates secreted by the reproductive tract, be it the seminal plasma of the male or the secretory fluids of the female, in regulating the metabolic behaviour of spermatozoa, in respect, at any rate, of those enzymatic reactions that are mediated by NAD-dependent sperm-dehydrogenases. At the same time, the determinations of the oxidized and reduced forms of NAD in spermatozoa provide a means for rapid recognition of extracellular metabolites potentially capable of undergoing oxidoreductive breakdown by spermatozoa.

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Autoradiographic Localization of ^{3}H-β-Ecdysone in Salivary Gland Cells of *Drosophila virilis*

ALTHOUGH the hormone ecdysone is known to initiate moulting and metamorphosis in insects its precise mechanism and site of action are unclear. When injected into larvae of *Chironomus tentans* it stimulated the formation of specific puffs in the polytene, salivary gland chromosomes[1], and two mechanisms have been proposed to explain this. Karlson and Sekeris[2] postulated that the hormone acts directly on the genome to "derepress" it, allowing the DNA to be transcribed. Kroeger[3-5], however, suggested that ecdysone activates a

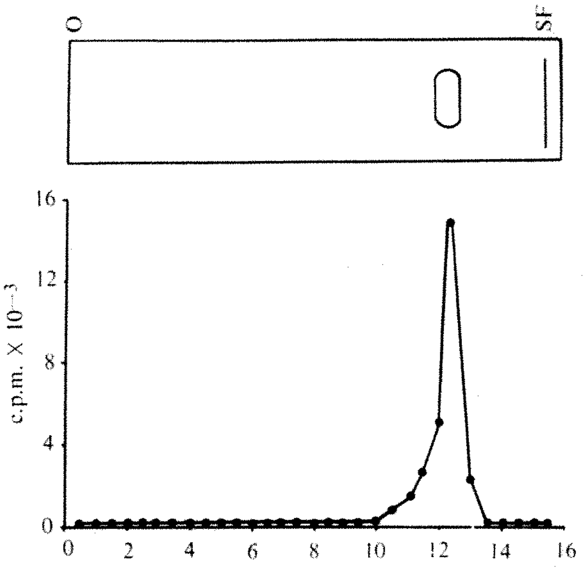

Fig. 1 Thin-layer chromatographic separation of authentic β-ecdysone (upper part of figure) and radiochromatogram of chloroform and ethanol extract of tissue incubated with ^{3}H-β-ecdysone for 30 min (lower part of figure). Silica gel HF 254+366 is the solid phase and ethanol : chloroform : water (70 : 20 : 2) is the solvent. O, Origin; SF, solvent front.

Selforganization of Matter and the Evolution of Biological Macromolecules

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sodium pump at the cell membrane. We have now investigated by autoradiography the distribution of ^{3}H-β-ecdysone in isolated salivary gland cells of *D. virilis*.

Salivary glands of *Drosophila virilis* were dissected from third instar larvae and incubated for 15–30 min in Ephrussi–Beadle medium[6] containing 10 μCi (1.6 μg) of ^{3}H-β-ecdysone (specific activity 3 Ci/mmol, New England Nuclear Corp.) or ^{3}H-progesterone (specific activity 10 Ci/mmol, New England Nuclear Corp.). After incubation, glands were washed in Ephrussi–Beadle medium, transferred to gelatinized slides and stained with lactic–acetic–orcein for 3–5 min. The glands were squashed under a siliconized cover slip, frozen between blocks of solid CO_2 and the cover slip removed. The tissue was fixed by immersing the slides in 10% formalin for 60 min. Kodak NTB-3 nuclear tracking emulsion was applied and the slides were stored in light-tight boxes for 40 to 70 days at 4° C. Autoradiographs were developed in Kodak D-19 developer.

To determine whether the silver grains were due to β-ecdysone or a metabolite, the tissue was incubated with ^{3}H-β-ecdysone for 30 min, homogenized and extracted with chloroform and ethanol. The extract was analysed by thin-layer chromatography (TLC) using silica gel HF 254+366 as the solid phase and ethanol : chloroform : water (70 : 20 : 2) as the solvent. The distribution of radioactivity was determined by scanning the TLC plate in a Baird Atomic radiochromatogram scanner, model RSC-363. In further experiments to detect any possible metabolites of ecdysone 0.5 cm sections were scraped from the plates, eluted with ethanol, and counted in toluene scintillation fluid. The radioactivity of the chloroform and ethanol extract (Fig. 1) co-chromatographed exactly with a sample of authentic β-ecdysone (Mann Research Laboratories). Thus there is no evidence that the silver grains were due to a metabolite of β-ecdysone.

Autoradiographs prepared from salivary glands incubated with ^{3}H-β-ecdysone showed that the radioactivity was concentrated over the nuclei and associated with the chromosomes (Fig. 2). In Fig. 2*A* the grains are arranged in a line over some of the chromosomes but are not concentrated at any particular gene loci. To test whether this was a specific concentration of the hormone, rather than nonspecific steroid binding, other salivary glands were incubated with ^{3}H-progesterone. There was no concentration of radioactivity from this steroid hormone over any area of the cell (Fig. 2*D*). These results tend to support the hypothesis that ecdysone acts in the nucleus but do not completely rule out the model proposed by Kroeger since silver grains are evident over other areas of the cells although less concentrated.

α-Ecdysone, first isolated from silkworm pupae[7], is thought to be the active moulting hormone in insects. The α-ecdysone analogue β-ecdysone (20-hydroxyecdysone, ecdysterone, crustecdysone) can initiate metamorphosis of wing disks of *Galleria mellonella*, stimulate evagination of imaginal disks of *D. melanogaster* cultured *in vitro*, induce puffs in salivary gland chromosomes and stimulate protein and RNA synthesis in various insects[8–12]. β-Ecdysone has also been reported to be significantly more active than α-ecdysone in inducing puparium formation in ligatured larval abdomens of Diptera[13,14]. Horn *et al.*[15] suggested that α-ecdysone is the

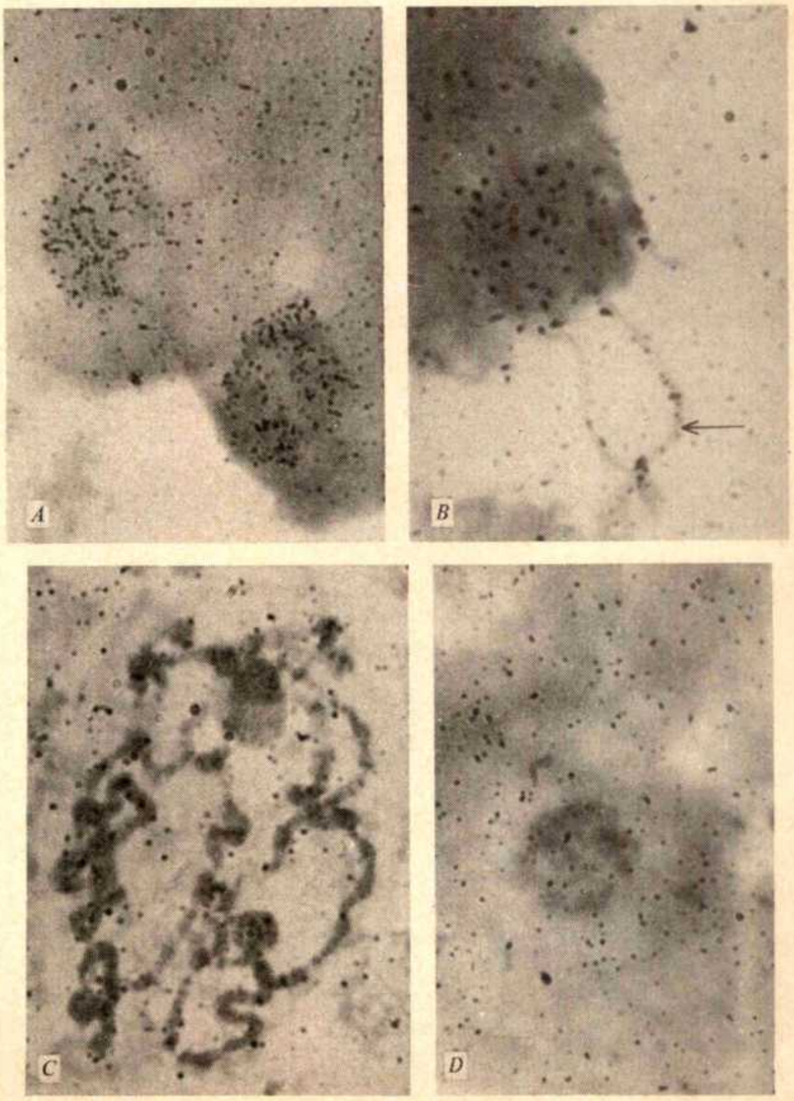

Fig. 2 Autoradiograms of squash preparations of *D. virilis* salivary glands. Glands were incubated *in vitro* with tritiated β-ecdysone (*A*, *B*, *C*) or progesterone (*D*). *A*, Silver grains are concentrated over two adjacent nuclei and some tend to parallel the underlying chromosomes (× *c*. 600). *B*, Note part of a chromosome protruding from the nucleus (arrow) (× *c*. 840). *C*, Silver grains associated with chromosomes (× *c*. 990). *D*, Note lack of concentration of radioactivity from progesterone over any area of the cell (× *c*. 600).

precursor of β-ecdysone, and this has recently been verified[16,17] for crustaceans and insects, which convert α-ecdysone to β-ecdysone within 15 min. They suggested that α-ecdysone is a very short lived intermediate in the synthesis of β-ecdysone.

Which ecdysone (if not both) is the active hormone in these insects? Our data showing that β-ecdysone is concentrated by nuclei of salivary gland cells and those reported by others suggest that α-ecdysone is converted to the more active β-ecdysone just as testosterone is converted to a more active metabolite, 5-α-dihydrotestosterone, in its target tissue[18-21]. Support for this hypothesis comes from the work of Thomson *et al.*[22], who found that β-ecdysone is also concentrated by the nuclei of the fat body of *Calliphora stygia*. Conflicting reports[23,24] make it unclear whether α-ecdysone is also concentrated by salivary gland nuclei.

Emmerich[25] has recently reported that proteins in salivary glands of *D. hydei* bind α-ecdysone. Our attempts to identify by standard techniques[26-29] specific cytoplasmic or nuclear "receptor" proteins in salivary glands of *D. virilis* which bind β-ecdysone have been unsuccessful. The mechanism by which β-ecdysone is concentrated by these nuclei remains to be determined.

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Effect of Prostaglandin E_1 on Adjuvant Arthritis

WE have found that when rats are treated with the prostaglandin PGE_1, adjuvant arthritis is prevented and suppressed. Although the treatment had no effect on delayed hypersensitivity to PPD, it reduced the immune response to sheep red blood cells (SRBC). Our findings support earlier indications that PGE_1 might modify the inflammatory response[1,2].

Adjuvant arthritis appears in rats 10–14 days after a single intradermal injection of Freund's complete adjuvant[3] and provides a convenient experimental model for *in vivo* evaluation of anti-inflammatory and/or immunosuppressive agents[4].

Adjuvant disease was induced in adult male Holtzman rats by intradermal injection into the left hind paw of 250 µg of steam-killed *Mycobacterium tuberculosis* in 0.05 ml. of heavy mineral oil. Three groups of rats received either 500 µg of PGE_1, 500 µg of prostaglandin A_2 (PGA_2) or buffer alone (0.06 M sodium phosphate buffer used to dissolve prostaglandins) subcutaneously twice daily for 21 consecutive days from the time of adjuvant injection (day 0). (Prostaglandins were a gift from Dr John Pike, Upjohn Company, Kalamazoo). Three groups received a similar 21 day course of PGE_1 beginning 7, 14 and 21 days after adjuvant injection. Severity of arthritis in the three uninjected paws was evaluated as described earlier[4].

The most pronounced side effect of prostaglandin therapy was somnolence within 5 min of injection and lasting about 2 h. Similar effects on the central nervous system have been noted in rats after administration of comparable doses of PGE_2[1]. Transient diarrhoea was observed sporadically. Diffuse alopecia, apparently unrelated to injection sites, developed in 5 rats treated from days 7 to 27.

Severe polyarthritis developed in all control and PGA_2-treated rats. Those treated with PGE_1 from day 0 and day 7 developed little or no arthritis; when treatment began on day 14 the typical explosive course of the arthritis, which had already

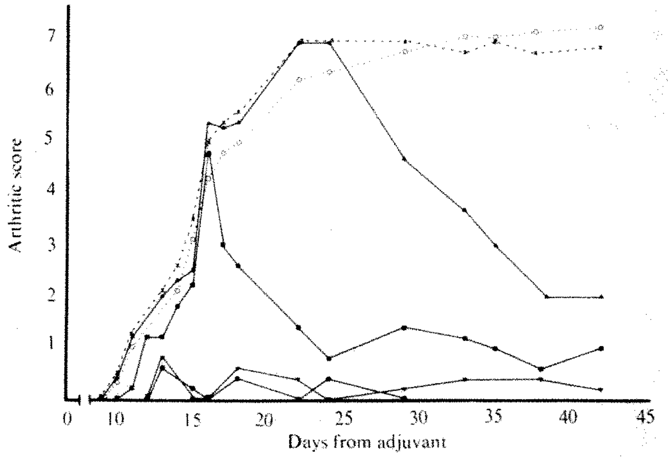

Fig. 1 Effect of prostaglandin on adjuvant arthritis. Each point represents the mean arthritic score for the three uninjected paws (five rats per group). Numbers in parentheses indicate period of treatment. ×, Controls; ●, PGE_1 (0–20); ▼, PGE_1 (7–27); ■, PGE_1 (14–34); ▲, PGE_1 (21–41); ○, PGA_2 (0–27).

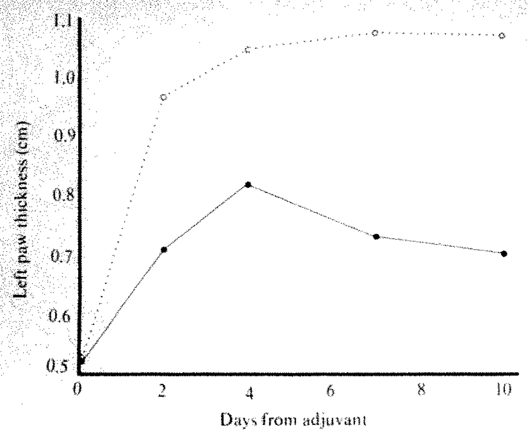

Fig. 2 Effect of prostaglandin on adjuvant arthritis. Each point represents the mean thickness of the adjuvant injected paw (five rats per group treated from day 0). ○, Controls; ●, PGE$_1$.

started, was suppressed. Established arthritis was considerably reduced even when treatment began on day 21 (Fig. 1). Arthritis did not develop in rats observed for 28 days after PGE$_1$ injections were stopped.

Rats treated with PGE$_1$ had a less intense inflammatory reaction at the site of adjuvant injection (Fig. 2), were more active and did not lose weight, nor develop the leucocytosis and anaemia characteristic of the disease and seen in the other two groups. The number of circulating lymphocytes was not diminished significantly by PGE$_1$.

On day 14, control and PGE$_1$ treated rats were tested with 10 μg of PPD, injected into the skin of the right ear. Buffer alone was injected into the skin of the left ear. Ear thickness was measured with a direct reading micrometer at 24 h intervals for 3 days. The delayed hypersensitivity reaction was positive in all rats, including those completely protected from arthritis. Erythema and induration were greater and more persistent in treated than in control rats (Table 1).

Table 1 Effect of PGE$_1$ on Delayed Hypersensitivity to PPD and Antibody Response to SRBC*

	Hours after PPD injection			Anti-SRBC titres
	24	48	72	
PGE$_1$	108†	210	189	8.72±0.49‡
Control	177	69	41	11.92±0.49

* Control and PGE$_1$-treated rats injected with 10 μg PPD into skin of ear, and 1 ml. 10% suspension SRBC intraperitoneally.

† Mean increase in thickness of the PPD injected ear minus thickness of buffer injected ear (five rats per group).

‡ Mean log$_2$ titre for each group of five rats 7 days after immunization, ±s.d.; $P<0.0005$.

Control and treated rats were given 1 ml. of a 10% suspension washed sheep red blood cells intraperitoneally on day 14, and were bled 7 and 17 days later for anti-SRBC titres to be determined[5]. The brisk antibody response seen in controls was reduced markedly in rats treated with PGE$_1$ (Table 1).

The mechanism(s) by which PGE$_1$ suppresses adjuvant arthritis is unknown but its biological effects suggest several explanations. A stimulatory effect on the pituitary-adrenal axis is suggested by the ability of PGE$_1$ to increase steroidogenesis[6–8]. In rats treated with paramethasone, however, polyarthritis developed within 7 days after treatment was stopped[9]. Such an "escape" phenomenon was not seen after treatment with PGE$_1$. There is experimental evidence that lysosomes can mediate tissue injury in joint disease[10]. The observation that PGE$_1$ reduces release of lysosomal enzymes from phagocytic cells *in vitro*[2] may be relevant to an anti-inflammatory activity *in vivo*. PGE$_1$ reduces uptake and degradation of aggregated bovine serum albumin by mouse macrophages[11]. It is possible that in the rat PGE$_1$ interferes with uptake and/or processing of antigen by macrophages. Antimacrophage globulin suppresses adjuvant disease[12] but arthritis appears within 2 days of termination of treatment. Arthritis did not appear after treatment with PGE$_1$ stopped, suggesting that an effect of PGE$_1$ on macrophages would be more permanent than simple inactivation of mature macrophages. PGE$_1$ inhibits phytohaemagglutinin-induced transformation of lymphocytes *in vitro* (unpublished results of R. Hischhorn), but another thymus-dependent function, delayed hypersensitivity to PPD, was not suppressed in treated rats. The reduction in the anti-SRBC titre suggests that an effect of PGE$_1$ on a restricted population of lymphocytes might contribute to suppression of adjuvant disease.

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Underwater and Aerial Visual Acuity in the Asian "Clawless" Otter *(Amblonyx cineria cineria)*

Gentry and Peterson[1] have compared data obtained from a sea otter (*Enhydra lutris*) on an underwater size discrimination task with data obtained by Schusterman *et al.*[2] using two sea lions (*Zalophus californianus*). Although Gentry and Peterson did not test the sea otter's vision in air, they concluded that its performance was inferior to that of the sea lion because the "pinniped eye" is emmetropic underwater with adaptations for aerial vision and that the "otter eye" (*Lutra*) was emmetropic in air with adaptations for underwater vision[3]. Such an interpretation of the difference between otters and sea lions emphasizes different dioptric mechanisms and ignores neural structure and organization at the retinal level, as well as at the level of the cortical projection areas.

Without determining that it can see better in air than underwater, the finding that the underwater visual acuity of the sea otter is poorer than that of the sea lion may have little connexion with their accommodative processes which are totally different[3]. Instead, the superior underwater visual acuity of the sea lion can be attributed to the superior resolving power of its retina. Although there has been no comparison of the detailed retinal structure and organization in otters and sea lions, the ratio of receptor to ganglion cells in sea lion retinas[4] is consistent with the finding that sea lions can resolve grating spacings subtending a visual angle of 5.5 minutes of arc both in air and underwater[5]. Tests of the behaviour of the ferret (*Mustela f. renata* and *Mustela cornine*a), a close relative of the otter, indicate that maximum visual acuity of these mustelids[6] in air is about one third that of the sea lion. Furthermore, the type of stimulus configurations initially used by Schusterman *et al.*[2] and subsequently by Gentry and Peterson[1] were relatively inappropriate for measuring visual acuity uncontaminated by intensity discrimination[5]. To resolve some aspects of these issues concerning the suitability of the visual systems of different aquatic mammals we tested the aerial and underwater visual acuity of two mature male Asian "clawless" otters (*Amblonyx cineria cineria*). These mustelids are widely distributed throughout south-east Asia. Their diet includes fish, frogs, crabs and birds, and they are reported to be used by the Malays for fishing[7].

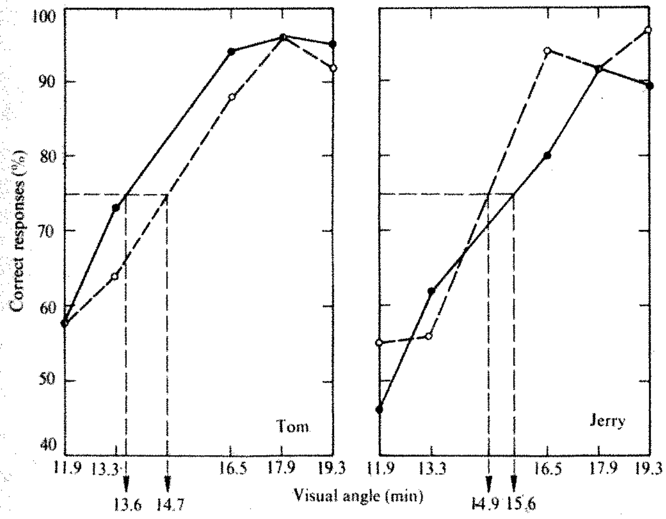

Fig. 1 The underwater (●) and aerial (○) visual acuity of otters (Tom and Jerry).

Both animals were trained and tested outdoors in a white plywood tank measuring 2.3 × 1.2 × 1.6 m. Detailed descriptions of the equipment and general procedures which were used are reported elsewhere[8,9]. Acuity targets were produced from 12.7^2 cm photos of Ronchi rulings with black and white stripes of equal width. The standard grating consisted of 300 lines per inch. The variable gratings consisted of lines varying in width from 12.7 mm to 4.8 mm. Targets were presented simultaneously by the experimenter lowering a target board from behind an opaque screen. The otters were maintained at a fixed distance of either 1.9 or 1.3 m from the targets with an opaque divider which projected down to the tank floor and outward from the opaque screen. The task was to approach the target with the variable grating in order to obtain a piece of chicken neck weighing 0.6 g. Once an animal left the start position after viewing the targets it was not allowed to retrace. If, after leaving the start position, an otter swam or ran to the side of the divider with the standard target it had to push that target; otherwise, the targets were withdrawn and the response was counted as an "error". The minimum distance between the gratings and the animal was taken as 1.9 or 1.3 m. Training and determination of a range of acuity targets were accomplished in a manner similar to that described for the testing of pinniped visual acuity[5,8,9].

Threshold estimates were obtained by the method of constants first used at a distance of 1.9 m with three variable targets subtending visual angles of 11.9′, 16.5′ and 19.3′ for 20 days and then at a distance of 1.3 m with variable targets subtending visual angles of 13.3′ and 16.5′ for 12 days. Each variable target was paired randomly with the standard for ten consecutive trials. Pairings were repeated twice for a total of sixty trials per day. Testing in air and underwater alternated daily.

Fig. 1 shows both aerial and underwater psychophysical functions for each otter. Thresholds may be found by noting the visual angles associated with 75% correct responses. These functions clearly show that the aerial and underwater visual acuity of *Amblonyx* is about the same. Threshold estimates measured in minutes of visual angle over the 16 test days were 13.6 and 15.6 for aerial acuity and 14.7 and 14.9 for underwater acuity. These figures are similar to those obtained on the aerial visual acuity of other mustelids[6].

These results suggest that it is not the totally different dioptic mechanisms (as has previously been suggested[1]) which account for the inferior underwater visual acuity of otters compared with sea lions and seals, but rather the poorer resolving power of the otter retina in combination with other neural elements including the cortical projection areas. Apparently, the dioptric mechanism of otters is such that it allows the eye to function normally in air without any special accommodative effort and is also capable of producing enough accommodation underwater[3] so as not to limit the visual acuity of the submerged otter.

Because it is supposed that the protopinnipeds were lacustrine and that they fed along the shores of streams, lakes or the sea, as do some modern otters, and because it has been suggested that the true seals may have descended from an otter-like ancestor[10], it is of considerable interest in terms of the evolutionary history of sensory systems of modern pinnipeds to compare the visual acuity of some otters with that of seals and sea lions. In spite of the limited data which are currently available it seems that the visual acuity of some pinnipeds[4,5,8,9] resembles more closely that of cats[4] than it does otters.

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Formation of a Carcinogen in Human Skin irradiated with Ultraviolet Light

THE role of ultraviolet light and sunlight in the aetiology of certain types of human skin cancer is now well established[1]. The mechanism(s) by which light induces such changes, however, are not understood. One explanation[2,3] of the induction of skin cancers by ultraviolet light and sunlight is that steroids in the skin are converted photochemically to carcinogenic materials, but failure to obtain such compounds by irradiation of naturally occurring sterols in biological systems has cast doubt upon the validity of such a hypothesis. Although Blum has argued against this hypothesis[4], he has recently described the induction by ultraviolet radiation of a diffusible substance that mediates hyperplasia[5]. Here we provide evidence for the formation of a cholesterol-derived carcinogenic photoproduct in human skin.

Table 1 Formation of Photo-oxidation Products in Skin

Treatment	Oxidation products*
Control	1.04
Irradiated (min)	
2	1.43
10	1.84
20	3.68
60	9.20

* Levels of polar photo-oxidation products were determined as the percentage radioactivity remaining at the origin of TLC plates, after development, from the total ^{14}C-cholesterol taken up by a unit weight of tissue. The yield of photo-oxidation products in the 60 min irradiated treatment is equivalent to approximately 26 ng/100 mg tissue. Note the relationship of photoproduct concentration to exposure time.

Skin obtained by surgery was immediately incubated in the presence of 5 μC of ^{14}C-4-cholesterol (specific activity 61.7 mCi/mmol) suspended in Krebs-Ringer phosphate buffer (*p*H 7.4) for 18 h at 4° C. The specimens were then thoroughly rinsed and irradiated in an environmental chamber maintained at 37° C with an ambient air atmosphere. Irradiation was accomplished with a Burdick QA-450N mercury arc lamp for periods of 2, 10, 20, and 60 min (1.34×10^5 ergs/s/cm^2). The chamber was fitted with a plane silica lens which transmitted all wavelengths emitted by the lamp (240–440 nm). Control specimens were maintained in identical conditions except that they were not irradiated.

After irradiation, the skin was cut into 50 μm sections with a freezing stage microtome and the total lipid was extracted as described before[6]. The total lipid fraction was chromatographed on silica gel coated thin-layer chromatography (TLC) plates. They were developed in 1,2-dichloroethane and the polar material remaining at the origin containing the cholesterol-derived photoproducts was eluted. Experimental details and chromatographic characteristics of skin photoproducts in multiple solvent systems will be published later. The amount of photoproducts formed was estimated from the percentage of the total radioactive cholesterol taken up by the tissue (Table 1). The photoproducts were co-chromatographed (TLC) with several reference oxidation products of cholesterol and developed in a chloroform-acetone (9:1) system. Good separation was obtained for all reference compounds except 7-ketocholesterol and cholesterol α-oxide which had the same R_F (0.83) values. The photoproduct fraction from skin migrating with the same R_F (0.83) as the two reference compounds was eluted and analysed by gas-liquid chromatography (GLC). A stream-splitter was placed in line with the flame ionization detector of the chromatograph. Cold reference compounds (7-ketocholesterol and cholesterol α-oxide) were added to the skin photoproduct fraction and the effluent from the split stream of the gas chromatographic column collected at 2 min intervals. As shown in Fig. 1 the profile of the major areas of radioactivity of the photoproducts, as eluted from the GLC column, and the chromatographic detector response are in agreement. The data, together with the TLC characteristics of both 7-ketocholesterol and cholesterol α-oxide, indicate that both compounds are present as constituents of ultraviolet-irradiated skin.

The mechanism involved in the formation of these photoproducts is unknown. One possible explanation is that photoproduct formation is the result of a primary photochemical oxidation. Alternatively photoproduct formation could be a result of the action of an intermediate oxidant on the sterol, that is, O_3, singlet oxygen and so on.

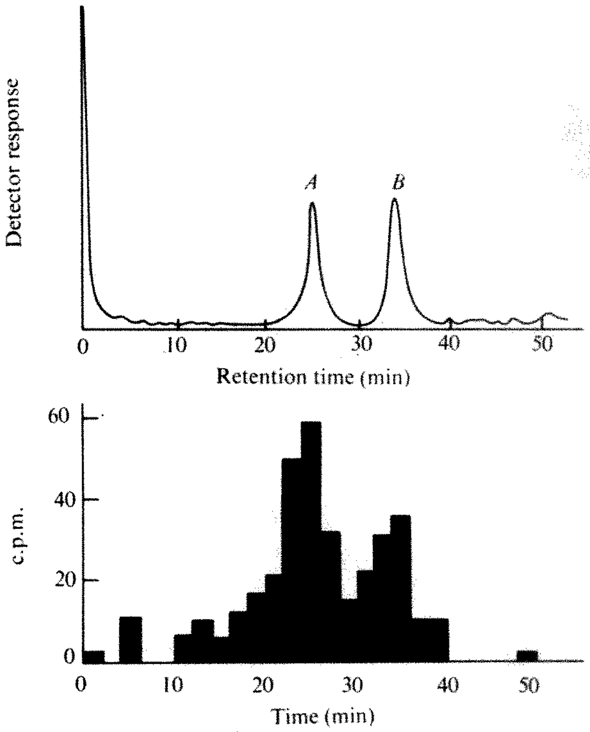

Fig. 1 Gas chromatographic record of (*A*) cholesterol α-oxide and (*B*) 7-ketocholesterol. Cold reference compounds were added to the TLC fraction of skin photoproducts demonstrating the same R_F value as these references. The histogram represents counts per minute (c.p.m.) of ^{14}C in sequential fractions of the gas chromatographic effluent. These data were obtained with the 60 min irradiated skin sample. The cholesterol α-oxide and 7-ketocholesterol fraction represented about 30% of the total photoproducts formed in skin.

Cholesterol α-oxide has been shown to be carcinogenic in both rats and mice and it is the only oxidation product of cholesterol to have carcinogenic properties in the absence of an oily vehicle[7]. As far as we know, this is the first report of light-induced formation of a carcinogenic compound from naturally occurring sterols in human skin. Studies are in progress to examine the potential relationship of photo-oxidation product formation to light-induced skin cancer.

This work was supported in part by a Robert A. Welch Foundation grant.

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Received May 27 1971.

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Visual-Auditory Distance Constancy

WE wish to describe a new perceptual constancy phenomenon which may be termed auditory distance constancy. If an observer views an event which produces a sound it seems that some compensation is made for the fact that the event will stimulate the eye somewhat before it will stimulate the ear depending on the distance of the event from the observer. For example, the sound of an event 35 m away will arrive at the ear about 100 ms after the light arrives at the eye.

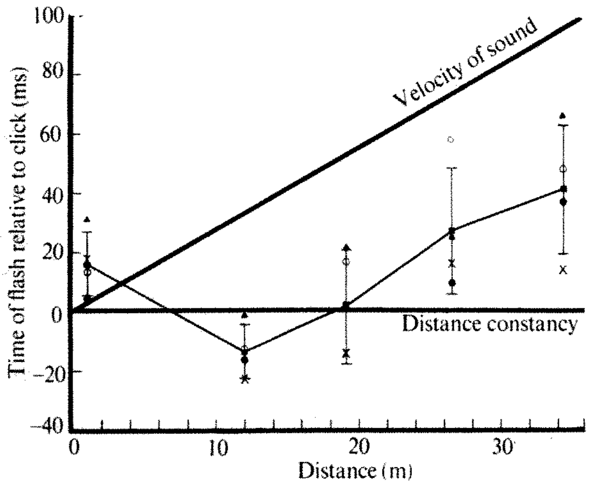

Fig. 1 Graph of the time delay of the flash relative to the click judged to represent a common event as a function of distance. Positive values represent the flash occurring after the click. ×, S_1; ●, S_2; ▲, S_3; ○, S_4; ■, mean.

To investigate whether compensation is made for differences in arrival time of light and sound we asked observers to judge whether a light flash and a click were simultaneous as a function of distance. The light was a model PS2E Grass photo stimulator mounted in a box whose front was 47 cm wide and 36 cm high. As seen by the observer, the front of the box contained a white square (15 × 5 cm) on a black background. The photo stimulator produced a brief illumination of the white square. The light box was set on a laboratory stool which was partly covered with a black cloth used to conceal a small loudspeaker. A 0.5 ms pulse fed to the speaker produced the click. Timing of the flash and the click was the function of two American Electronics Laboratories stimulators.

For the experiment an observer was seated at one end of a long corridor and the light box and speaker were located at various distances down the corridor. The corridor gave good distance cues. The light flash and click were presented with various delays between the flash and the click. The delays of the flash relative to the click were −200, −150, −100, −50, 0, 50, 100, 150 and 200 ms. (A positive delay means the click occurred before the flash.) The observer was asked to adopt the attitude that the click and the flash would ordinarily be the same event. Thus for a given click–flash combination he had to decide whether the combination met the criterion of representing a single event. The distances used in the experiment were 1, 11.9, 19.2, 26.5 and 34.4 m. Four observers were used in the experiment. For two observers each click–flash delay was presented ten times at each distance. For the other two observers each combination was presented fifteen times.

The results of the experiment are shown in the graph of Fig. 1. The ordinate represents the average delay of the flash relative to the click judged by each observer to represent a common event at each distance. The abscissa represents the distance at which the observation was made. A line is drawn through the mean delay for all four observers. Also shown is the standard deviation of the observers.

In addition to the observed data two theoretical lines are shown in Fig. 1. The horizontal line through zero delay represents the observations that would be obtained if the observers took perfect account of distance and the velocity of sound. The increasing straight line function represents observations that would be obtained if the observer took no account of distance and velocity but based their judgments on the simultaneous arrival of the sound and light at the observer. For this line the velocity of sound was taken as 344.45 m s^{-1} (calculated for dry air at 22° C). By comparing the observations with the two theoretical lines it may be seen that the observers corrected for the velocity of sound for distances up to about 20 m beyond which the constancy begins to break down. Even at 35 m, however, there is still compensation by a factor of 0.5. As to the pattern of observations at the shorter distances it is difficult to say whether the apparent undercompensation at 1 m and overcompensation at 11.9 m is genuine or due to peculiarities of the situation.

A further observation worth noting on the graph is that the standard deviations of the observers' means at various distances are fairly small ranging from 9 to 22 ms. On the other hand, the standard deviation for individual observers at each point ranged from 50 to 100 ms. Thus the variability of the observers relative to one another was about half that which would be expected on the basis of the individual variability. Although judgments of perceived simultaneity are typically in the region of 50–100 ms, this would not explain the small between-observer variability. We believe that the reason for the discrepancy between individual and group variability is that the distribution of judgments for an individual at a given distance may be bimodal, one mode corresponding to simultaneity of the flash and click at the observer and one to simultaneity at the source. To establish this, however, would require more careful measurements and longer distances.

Because the experimental results implied that observers compensated only partially for longer distances, a size constancy experiment was carried out to get estimates of the perceived distances. That is, the partial compensation could have resulted from underestimating the distances involved. The estimates were obtained by having each observer adjust a variable size white square on a black background, viewed at a standard distance of 3 m, to match the absolute size of the white square in the light box as a function of the distance of the light box. The settings of the comparison square relative to the true size of the square on the light box were used to estimate the perceived distance of the light box. It was found that in general the perceived distances matched the true distances very well and that in no case would the observer's error in distance perception account for failure to compensate completely for the auditory time delay.

This work was supported by a National Research Council of Canada grant to G. R. E.

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Received May 28; revised June 25, 1971.

CORRESPONDENCE

Environment Conference

SIR,—I should like you to know how much I appreciated the coverage of the Canberra meeting of SCOPE on September 1–3[1]. I must point out, though, that your correspondent entirely misunderstood the main thrust of my remarks on the question of the organization of environmental activities within the UN system. Far from advocating the creation of a "new agency", I specifically pointed out that environmental affairs do not lend themselves to the creation of another new specialized agency because they involve the interaction of a number of cause and effect relationships which transcend the traditional boundaries of sectors and institutions. I emphasized that we are still at too early a stage in our consideration of this important question to know what decisions governments will take concerning it at Stockholm. In outlining my own views as to the present state of thinking by governments, I made two points: (1) that some form of continuing machinery will be needed at the international level after the Stockholm Conference to follow up the decisions taken at Stockholm, and (2) that what is required principally is a better means of coordinating and providing a central forum and a concerted sense of direction to the environmental activities of the existing international organizations, rather than a new specialized agency.

I have set out here a list of the criteria which should, in my view, as I said at Canberra, be applied in determining the kind of international organizational arrangements that may be made following the Stockholm Conference. As these have been accepted in principle by the Preparatory Committee of twenty-seven governments set up by the UN General Assembly, and I believe are fully compatible with the views of the UN agencies concerned, they represent a reasonable indication of present thinking on this important subject. (a) Any organizational arrangements should be based first on agreement about what needs to be done. Until this is reached, no firm decision can be made on the ways and means to be adopted. (b) All functions that can best be performed by existing organizations should be assigned to those organizations, both international and national, most capable of carrying them out effectively. No unnecessary new machinery should be created. (c) It is more logical to consider a network of national, international, functional and sectoral organizations with appropriate linkages and "switchboard" mechanisms, whereby international organizations supplement and complement national organizations, than to think in terms of a global "super agency". (d) Any action envisaged should allow for the preliminary state of knowledge and understanding of environmental problems, and should be flexible and evolutionary. (e) Governments will want to attach highest priority to the need for coordination and rationalization of the activities and programmes of the various international organizations active in the environmental field. This is essential in order to avoid overlap and duplication and to assure most effective use of scarce resources of money and manpower. (f) Any policy centre that is expected to influence and coordinate the activities of other agencies should not itself have operational functions which in any way compete with the organizations over which it expects to exercise such influence. (g) In the establishment of any additional or new machinery it is essential to provide strong capability at the regional level. (h) The United Nations should be the principal centre for international environmental cooperation. (i) The organization of environmental activities within the United Nations should be so designed as to strengthen and reinforce the entire United Nations system.

While there can be and no doubt will be differences of view both in the UN family and amongst governments concerning the specific decisions which must be taken at Stockholm in applying these criteria, the degree of consensus that has already been achieved is a hopeful sign that these differences will be resolved successfully. The basic purpose of the preparatory process preceding Stockholm is precisely to enable all the relevant views to be fully discussed and reflected in the decisions governments will be asked to take at Stockholm.

Yours faithfully,

MAURICE F. STRONG

Secretary-General
of the Conference

United Nations Conference
on the Human Environment,
Stockholm

[1] *Nature*, **233**, 81 (1971).

Responsibility and the US National Academy

SIR,—In the November 5 issue of *Nature* (**234**, 7; 1971) there was a fairly extensive report of the reaction of the National Academy of Sciences to my resignation from that august body. In amplification of that report I would like to make a minor and a major point. The minor point is that I am *in fact* no longer a member of the National Academy, having ceased to be a member on the day of my resignation. Whether the Academy chooses or does not choose to accept my resignation is of no consequence. As I wrote recently to the President, "Membership in a voluntary association demands consent. I have withdrawn my consent".

The major issue concerns the meaning of responsibility. Apparently reports of the NAS–NRC in the future will carry a disclaimer of responsibility by all members of the Academy except for those who may have actually served on the working committee. It is suggested by your correspondent that this goes some significant way toward meeting my objections to the Academy's secret research. No one who is not either politically naive or Machiavellian can subscribe to such a view. "Responsibility" means both literally and in practice that one is in a position to be "called to account". Thus, responsibility inheres in a social relation and is defined by those who will do the calling, not by those who are called. It would be very convenient, of course, if each of us could define for himself when he was or was not responsible. Perhaps I could put a large sign on my car saying "This car is none too reliable and I will not be responsible for anyone killed by it". Mr Eichman said he only made up train schedules and was not responsible for what happened to people at the other end of the line. But Mr Eichman's victims and their families called him to account. It was they who defined the responsibility. The fact of responsibility cannot be waved away by wishful thinking. The facts are: (1) The National Research Council is the "operating arm of the National Academy". (2) The President of the Academy heads the National Research Council. (3) Officers of the National Academy have the power to determine policy of the National Research Council. (4) According to a letter from the President of the Academy, "The prestige of the National Academy of Sciences is used to recruit working Committees of the National Research Council". (5) The prestige of the National Academy stands behind every report and, indeed, every report has been reviewed by a special committee of the Academy.

Thus the Academy *is* responsible and no legal fiction of its own devising will change that fact. The best the members of the Academy can hope for is that accounts will not be called in their lifetime, or, if events move more swiftly, that the National Academy will be seen, in retrospect, as unimportant.

Yours faithfully,

R. C. LEWONTIN

University of Chicago

Fulfilling Fulton

SIR,—I was struck by the headline "Fulton Fulfilled" in your issue of October 8 (*Nature*, **233**, 365; 1971). I have only now seen it on my return from holiday, and I wondered what exciting civil service developments I had missed.

The introduction of an interim Science Category, satisfactory in structure terms but with pay arrangements that, despite our success in improving on the arbitration award, are still wholly unsatisfactory, is a long way indeed from the fulfilment of Fulton.

There is the question of pay. The Institution did not accept that pay research was valid for scientists, and we refuse now to believe that they can reasonably be paid less than technologists or administrators. We are determined that we shall not again have pay research applied in an area where it is so clearly inapplicable. We shall redouble our efforts over the coming months to find a relevant basis for the pay of scientists. Then there is the question of careers; as I believe, the most important issue of all. On that, we are currently engaged in discussions with the Civil Service Department, and I am optimistic that we shall make real progress by the spring of next year.

Yours faithfully,

CYRIL COOPER

Deputy General Secretary

The Institution of Professional
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Northumberland Street,
London WC2N 5BS

Population and Economics

SIR,—I suppose that your highly irresponsible editorial of November 5 (*Nature*, **234**, 2; 1971) under the heading "Alice Economics" need not be considered seriously, but there is a danger that what you have written will be read by "young people and other innocents", to use your own phrase in the other context. Professor Scorer, whose views you criticize, is not the only one to draw attention to the ecological predicament which will be speeded up by an expansion of EEC, and it is a pity that you can do no more than poke fun of him; indeed the fact that you do this indicates your own uneasiness.

You suggest that Professor Scorer's premises are false by taking a series of examples. Thus you ask if it is an accident that the richest nation on Earth is the one most concerned about pollution. No, it is not an accident, but must we industrialize and pollute every nation in the world before we become interested in the problems we are creating? You also ask if there is anything but economic growth that will free India of cholera. To free India of cholera would simply add a few more to the 14 or so million people that India is adding to the world every year. Economic growth cannot possibly help India and similar countries: if everyone in the world enjoyed the same standard of living and consumption as the average Londoner, the world's resources would disappear almost instantaneously. Indeed economic growth in the EEC and other industrial groupings will do nothing for India and the many other desperate nations except to encourage them to sell their dwindling raw materials even more rapidly to the expanding industrial complexes which so many see as a solution to all economic difficulties. Professor Scorer may be wrong as to why the resources of the sea are not as rich as they used to be. You think that over-fishing is the problem, he suggests pollution. You may both be right, but the common denominator is expanding human numbers and, especially in Europe, expanding human needs.

To argue that entering the EEC is anything more than a conspiracy to create opportunities for big business is misleading. The expanded economic unit will demand more and more resources from the under-developed world, whose populations are likely to continue to increase at a phenomenal rate, thanks to the "aid" we offer as a small token of our appreciation for their help. You may think this a joke, but have you considered that, taking into consideration the resources it will consume, every child born in England, Sweden or America is forty or fifty times the ecological disaster of one born in Ghana, Sierra Leone or Liberia?

Yours faithfully,

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Tax on Pollution

SIR,—The recently reported claim of the salvage industries to be given zero rating for value-added tax may not only attract wide support but can also be extended. The operation of VAT will automatically provide the machinery for a pollution-added tax, PAT, either as part of VAT or alongside it. By this means, the visible cost of each manufacturing process can gradually be made to include the social cost of the stress it imposes on the environment, and the price of a product can be made to cover the cost of its salvage, re-cycling or disposal.

Restrictive legislation, although a necessary adjunct, is widely recognized to be insufficient of itself to control environmental deterioration; it is too blunt an instrument, the enforcement of which is necessarily ponderous, expensive and therefore sporadic. PAT by contrast can provide effective economic pressures operating in detail day by day. Its application can be flexible, selective and finely graduated. Since rating for PAT would be subject to appeal based on expert testimony, it provides economic motivation for research aimed at elucidating the real effects of pollution and ecological disturbance. This knowledge is an essential prerequisite of right action in the preservation of our living environment.

Yours faithfully,

PETER FELLGETT

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Reading RG6 2AL

Announcements

University News

Dr W. G. Irwin has been appointed to the chair of general practice, **Queen's University of Belfast.**

Dr B. Benjamin, Civil Service College, has been appointed visiting professor of applied statistics in the Graduate Business Centre, **City University.**

Mr G. T. Goodman, University College, Swansea, has been appointed to the chair of applied biology tenable at Chelsea College, **University of London,** and **Dr O. M. Wrong,** University of Dundee, has been appointed to the chair of medicine tenable at University College Hospital Medical School. The title of professor of nutrition has been conferred on **Dr A. E. Bender,** in respect of his post at Queen Elizabeth College.

Appointments

Dr Lionel E. Mawdesley-Thomas has been appointed director of the **Huntingdon Research Centre.**

Mr H. A. Maxwell, Professor D. H. Valentine, Mr Hew Watt, Professor A. D. Bradshaw and **Professor C. D. Pigott** have been appointed members of the **Nature Conservancy,** in succession to **Sir Henry Beresford-Pierse, Mr R. B. Verney, Professor R. O. Buchanan, Professor A. R. Clapham** and **Sir Charles G. Connell. Mr A. E. Smith** has succeeded **Mr R. B. Verney** as chairman of the Conservancy's Committee for England and **Professor K. M. Clayton** and **Mr Stanley Cramp** have joined the Committee, from which **Professor J. T. Coppook, Dr S. M. Walters** and **Mr J. R. Herbert** have retired.

Miscellaneous

Entries are invited by the **Plastics and Polymer Group of the Society of Chemical Industry** for the annual prize of £50, awarded for the best paper received on any aspect of pure or applied polymer science. Entrants who are not British subjects must be overseas members of the Society, and the entries should be between 3,000 and 5,000 words and in English. Further information is available from the Plastics and Polymer Group, Society of Chemical Industry, 14 Belgrave Square, London SW1X 8PS.

A travelling scholarship of £300 is offered by the **Institute of Electrical and Electronics Engineers** for a visit or visits to foreign electrical or electronic research or manufacturing establishments by a postgraduate student. Candidates must submit a programme for their visits by December 31, and must be students or graduate members of the Institute of Electrical and Electronics Engineers, the Institution of Electrical Engineers or the Institution of Electronic and Radio Engineers. Further information is available from Dr A. J. Ellison, Queen Mary College, Mile End Road, London E1 4NS.

Applications are invited by the **International Agency for Research on Cancer,** Lyon, for training fellowships in 1972–73. The fellowships are awarded for one year and are tenable at a suitable institution abroad. Applicants should be junior scientists who intend to pursue a career in cancer research and who wish to be trained in such research, and the agency is particularly interested in receiving applications for training in epidemiology, biostatistics and all aspects of environmental biology. Further information can be obtained from the chief of the Research Training and Liaison Unit, International Agency for Research on Cancer, 16 Avenue Marechal-Foch, 69 Lyon (6e), France. Applications must reach the agency not later than February 29, 1972.

The 1971 awards of **State Prizes of the USSR** for science and technology include: **L. D. Fadeev,** for his work on the non-relativistic quantum theory of the scattering of charged particles; **E. P. Aksenov** and **G. N. Duboshin,** for their work on the perturbed motion of natural and artificial satellites and of asteroids, and on the formulation of the Earth's gravitational field; **Academician L. A. Artsimovich** and his team for their theoretical and practical work on high-temperature thermonuclear plasma; **Corresponding-Academician D. I. Blokhintsev** and his team for work on the new fast-neutron impulse nuclear reactor; **G. I. Goretskii,** for geological work connected with major hydro-electric projects; **S. A. Popov, T. M. Mukhamedov** and their team for investigating the engineering problems involved in the Bakhsh irrigation scheme in Tadjikstan; **Yu. A. Eliseev** and **A. V. Karagin** for innovations in building technology; **G. E. Ovsepyan** and his team for development of the "Nairi" computer; **T. M. Zakharenko, A. K. Miloserdnyi, I. K. Pokhodnya, N. V. Panyushkin, V. Kh. Kas'yan, I. I. Kershanskii, I. P. Brovin, P. D. Borodin, A. I. Antonov, F. S. Borisov, I. A. Figurovskii, G. B. Karapetyan, V. L. Arkhangelskii, I. M. Petukhov, S. G. Avershin** and their teams for specific innovations in industry; **Academician G. A. Razubaev** and **N. S. Byazankin** for work on the synthesis of metallo-organic compounds; **K. K. Andreev** and **A. F. Belyaev** for theoretical work on the combustion of explosives; **G. P. Badalov, Ya. A. Timoshenko, A. T. Vorontsov, E. I. Zakharova** and their teams for the development of agricultural machinery; **Academician N. D. Ierusalimskii, Corresponding-Academician G. K. Skryabin** and their teams for work on the production of nutrient protein from petroleum wastes; **F. V. Krogius** and his team for their detailed study of the ecology of Lake Dalnoe (Kamchatka); **E. V. Shmidt** and his team for work on the major vessels of the brain; **Academician B. V. Petrovskii, Dr V. I. Shumakov** and their team for the development of kidney transplants; **A. P. Andriyashev, E. I. Tolstikov** and their team for their "Atlas of Antarctica"; **Corresponding-Academician R. I. Avanesov** and his team for their work on the linguistic geography of Byelorussia; **A. P. Dul'zon** and his team for their work on the Ket language of Western Siberia and the ethnology of the area; **T. Kh. Margulova** for her book *Atomic Power Stations,* and **A. P. Kreshkov** for his book *Principles of Analytical Chemistry.*

International Meetings

January 3–5, 1972, **The Teaching of Numerical Analysis,** Brighton (The Secretary and Registrar, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

January 4, 1972, **Plant Constituents of Pharmacological Interest,** London (Dr J. B. Harborne, Botany Department, The University, Reading RG1 5AQ).

January 4–5, 1972, **Incineration of Refuse and Sludge,** Southampton (Mr M. A. McSweeney, Symposium on Incineration of Refuse and Sludge, Department of Civil Engineering, University of Southampton, Southampton SO9 5NH).

January 4–6, 1972, **Solid State Physics,** Manchester (Meetings Officer, Institute of Physics, 47 Belgrave Square, London SW1).

January 5, 1972, **Vibration Isolation,** London (Society of Environmental Engineers, 68a Wigmore Street, London W1H 9DL).

January 5–7, 1972, **Design of Laboratories for Work with Toxic and Biological Materials,** Leeds (Director of Special Courses, Department of Adult Education and Extramural Studies, The University, Leeds LS2 9JT).

January 7, 1972, **Sampling of Mineralogical and Geological Materials,** London (The Editor, Institution of Mining and Metallurgy, 44 Portland Place, London W1N 4BR).

January 7–8, 1972, **Blood Flow Measurement,** London (Dr V. C. Roberts, Department of Biomedical Engineering, King's College Hospital Medical School, Denmark Hill, London SE5).

January 10–11, 1972, **The Molecular Basis of Biological Transport,** Miami (Biochemistry-PCRI Winter Symposia, PO Box 906, Biscayne Annex, Miami, Florida 33152, USA).

January 10–12, 1972, **Surface Physics of Semiconductors,** Southampton (Meetings Officer, Institute of Physics, 47 Belgrave Square, London SW1).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

The World Land Use Survey. Occasional Papers, No. 10: Contributions to Land Use Survey Methods. Edited by Hans Boesch. Pp. 63. (Berkhamsted, Herts: Geographical Publications Limited, 1971.) £2.50. [48

Shoe and Allied Trades Research Association. Annual Report 1970. Pp. 108. (Kettering: Shoe and Allied Trades Research Association, 1971.) [48

About Patents: Patents as a Source of Technical Information. Pp. 21. (Orpington, Kent: Sale Branch, The Patent Office, 1971.) *gratis*. [48

Science Research Council. Support of Enzyme Chemistry and Technology, 1969–71. Pp. 12+xii. (London: Science Research Council, 1971.) [48

Natural Environment Research Council. Culture Collection of Algae and Protozoa—List of Strains. Pp. 73. (Cambridge: Culture Centre of Algae and Protozoa, 1971.) [58

Building Research Station Digest No. 132: Wilful Damage on Housing Estates. Pp. 4. (London: HMSO, 1971.) 5p. [98

Political and Economic Planning. Broadsheet No. 529. . . . and Now the Future: a PEP Survey of Future Studies. By Charles de Hoghton, William Page and Guy Streatfield. Pp. iii+171. (London: PEP, 1971.) £2. [98

Department of Trade and Industry. Safety in Mines Research 1970: Forty-Ninth Annual Report of the Safety in Mines Research Establishment. Pp. 90+4 plates. (London: HMSO, 1971.) 60p net. [108

Bulletin of the British Museum (Natural History). Botany. Vol. 4, No. 7: A Survey of the Tropical Genera *Oplonia* and *Psilanthele* (Acanthaceae). By W. T. Stearn, Pp. 259–323+plates 38–47. £2.60. Entomology. Vol. 26, No. 3: A Revision of the Genus *Canaea* Walker (Lepidoptera, Thyrididae). By P. E. S. Whalley. Pp. 159–179+12 plates. £1.40. (London: British Museum (Natural History), 1971.)[108

Association International d'Oceanographie Physique. Publication Scientifique No. 29: Bibliography on Mean Sea Level 1959–1969. Bibliography on Tides 1955–1969. Pp. 40. (Birkenhead: Permanent Service for Mean Sea Level, Institute of Coastal Oceanography and Tides, 1971.) £1.50. [108

Department of Health and Social Security Annual Report 1970. (Cmnd. 4714.) Pp. xxiv+383. (London: HMSO, 1971.) £2.80 net. [108

Smith Kline and French Foundation. Eighth Annual Report 1970. Pp. 8. (Welwyn Garden City, Herts: Smith Kline and French Foundation, 1971.) [118

Metrics: a Guide to Metrication Information and Sources. Pp. 27. (London: London Borough of Lewisham, Technical Reference Library, 1971.) *gratis*. [128

Natural Environment Research Council—Institute of Geological Sciences ICSU/SCOR Working Party 31 Symposium, Cambridge 1970—The Geology of the East Atlantic Continental Margin. 1: General and Economic Papers. (Report No. 70/13.) Pp. v+175. 90p net. 2: Europe. (Report No. 70/24). Pp. iv+170. 90p net. 3: Europe (continued). (Report No. 70/15.) Pp. v+106. 60p net. 4: Africa. (Report No. 70/16.) Pp. iv+209. £1 net. (London: HMSO, 1971.) [128

The Zoological Record. Vol. 105, Section 18, 1968: Aves. Compiled by the Staff of the Zoological Society of London. Russian literature compiled by Professor A. I. Ivanov. Pp. vi+262. £3. Vol. 106, Section 7, 1969: Brachiopoda. Compiled by the Staff of the Zoological Society of London. Pp. v+25. £3.50. (London: Zoological Society of London, 1971.) [138

Other Countries

Australia: Commonwealth Scientific and Industrial Research Organization. Research Report of the Division of Nutritional Biochemistry for the year 1970. Pp. 70. (Adelaide: CSIRO, 1971.) [287

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Mechanical Engineering, 1969–1970. Pp. 67. (Melbourne: CSIRO, 1971.) [287

Smithsonian Contributions to Zoology. No. 72: Revision of the Fish Genus *Ecsenius* (Blenniidae, Blenniinae, Salariini). By Victor G. Springer. Pp. 74. $1.25. No. 73: Synopsis of the Tribe Salariini, with Description of Five New Genera and Three New Species (Pisces: Blenniidae). By William F. Smith-Vaniz and Victor G. Springer. Pp. 72. $1.25. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office.) [297

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Rothschild vs Dainton (Contd)

MANY of those who will have listened to Lord Rothschild's speech to the Royal Society of Arts on Wednesday (see page 319) will be rubbing their hands with glee, saying that he has gone too far this time. Surely, the argument will go, it is not possible to make fun in the same speech of Lord Haldane, Professor John Archibald Wheeler of Princeton University, the proton accelerator at Batavia in Illinois and the British research councils. Is it really possible to go about mocking at respected parts of the established world of science and then persuade respectful personages such as the Permanent Secretaries of British government departments, not to mention the British Prime Minister, that the time has come for radical change in the way in which civil science is financed in Britain ? The trouble is that for all the huffing and puffing which there has been in university common rooms in the past few days, there is every reason to think that Lord Rothschild's attack on the established way of things is not merely vigorous but shrewd. For one thing, there are serious flaws in the present organization of the research councils, and those who wish to defend the present system would be in a stronger position if they would confess as much. Second, there are reasons for thinking that government departments are less expert than they might be in dealing with modern problems by modern methods because of the separation between science and state first insinuated by the Haldane committee and its interpreters. Third, to choose this point in the political history of Britain for a plea for stronger control by customers of how public money is spent is likely to warm the cockles of a great many hearts in the present government, which means that Lord Rothschild is in a strong tactical position. But, finally, it is also a good time for raising afresh the question of what the contribution of scientific research to public life is meant to be. Those who pretend otherwise, and who ignore such things as the complaints of the general public about the malevolence of technology and the unwillingness of young people to enter science courses at university, are on shaky ground.

How has the scientific community been caught so obviously on the wrong foot ? After all, the question of reorganization has been in the air for more than a year, and especially since Sir Solly (now Lord) Zuckerman advocated that the Agricultural Research Council should be financed from the budget of the Ministry of Agriculture. That was a shot across the bows, to say the least of it. For all the zeal with which the Council for Scientific Policy has responded, and for all the merits of Sir Frederick Dainton's report (see *Nature*, **234**, 169; 1971) which eventually saw the light of day at the same time as Lord Rothschild's pronouncement, it remains a simple truth that the defence of the research councils, for what it may be worth, has been badly mishandled. First of all, the members of Sir Frederick Dainton's committee have spent much of the past year complaining that the government would not publish Sir Frederick Dainton's report. Why was none of them willing to take the government by surprise, and agree to let the cat out of the bag? If the text of the Dainton report had found its way into print, however irregularly, before the beginning of October, its impact would have been stronger. But the document would even now carry greater weight if it made fewer compromises with the past and present. And it is unconvincing to suggest, as the Dainton committee does, that the future pattern of the research councils should be allowed to evolve under the aegis of a board including *ex officio* the President of the Royal Society no less, which would from time to time have created new research councils or have strangled others to death. Such a device is not merely a reaffirmation of the separation between government departments and scientific research which is supposed to stem from Haldane but could in principle consist of a further separation between the government and research policy. It would have been much better if the Dainton committee had grasped some of the nettles which have grown up within the research council system. Is it right that the Natural Environment Research Council should continue to exist ? Should the research councils in agriculture and medicine pursue a policy of setting up research units separately from universities but without explicit connexions with the requirements of government policy ? What, in any case, can be said about the scale on which these efforts should be carried out? But the Dainton report would also have been a stronger document if it had made fewer obvious concessions to the climate of opinion which has been created by the arrival of the present government in office. The arrangements suggested for liaison between the board of management of the research councils and the other government departments are, after all, in many ways incompatible with the stark interpretation of the Haldane principle. The greatest failing, however, is that even now the scientific community is for practical purposes saying nothing about the issue. Its champion is Sir Frederick Dainton and his enemy is Lord Rothschild. Sir Frederick can count on the warm friendship and fond admiration of his colleagues in the laboratory, but he will be exceedingly lucky if any of them speaks out in public.

It is therefore important to acknowledge that in some respects Lord Rothschild has indeed gone too far. First of all, his argument on the functions of scientific research is incomplete. He said on Wednesday this week that basic research has no definable function but that, of course, is quite mistaken. Even if he is right to argue that the adventitious benefits which stem from basic research have no place in the kinds of calculations which governments must make—if only governments would listen more carefully to this advice, they would less frequently be led to spend money on white elephants for the sake of what they are pleased to call spin-off—he is wrong to ignore the part that scientific research has to play in higher education. For one thing, teachers cannot teach well, and many will not teach, if they have no opportunity for research.

Second, universities which live far back from the limits of understanding tend to be unstimulating universities. Third, students cannot become creative scientists without cutting their teeth on research of the kind carried out in good university laboratories. And even if it should happen that the supply of PhDs exceeds the demand that comes simply from university teaching laboratories, not merely is there very little danger that the people concerned will finish up as lift attendants (as Lord Rothschild said) but there is no way of knowing in advance just which shiny-eyed undergraduate will turn out to be good at research. It is conventional in Britain for educationists to oppose selectivity at the age of eleven, and there is a growing tendency to complain about the rigours of university entrance, but nobody yet takes seriously the much more apparent truth that it is hard to guess at an experimentalist's flair from reading his undergraduate essays. In short, a sufficient justification for a substantial amount of basic research is that it is inseparable from higher education. Moreover, this part of the argument in defence of the research councils (or at least the Science Research Council) is in principle quantifiable. Is it entirely beyond the wit of the Council for Scientific Policy, whether it likes it or not, now cast in the role of the defender of the research councils, to do some hard thinking on this point before the date on which the government has said it will close its ears to further discussion, February 29, 1972.

Lord Rothschild is also on dangerous ground in his description of how government departments should assume the unfamiliar role of customers, with money jingling in their pockets to spend on applied research. One immediate difficulty is that the structure of government departments is necessarily inward looking. In the nature of things, Permanent Secretaries are unwilling to pay outsiders for services rendered when they can, in principle at least, provide the same services for themselves. This, after all, is why the British defence research establishments have flourished so prodigiously. What reason does Lord Rothschild now have to think that the Ministry of Agriculture will willingly spend money on research contracts with the Agricultural Research Council when it could do the same work, perhaps less well, at its own laboratories? Is there not a danger, even, that the research councils will be lumbered not with the long-range work, applied in character though it may be, which has been its stock-in-trade so far, but rather with the humdrum work which nobody particularly wants to do? In other words, there is a danger that the customer-contractor relationship, logical enough on paper, may be unworkable in practice. Certainly it could not work without far-sightedness on the part of government departments of a character so far conspicuously absent, and without receptiveness on the part of the research councils, improbable now that they are all smarting from injured pride. This is why the only practical response to Lord Rothschild's document is a carefully planned experiment in research by customer-contractors. The Agricultural Research Council is the place to start. Plant breeding is an obvious subject. To suggest more than this for 1972–73 would be a folly. To agree to less would be churlish.

Lord Rothschild has also skated over thin ice in what he has to say about the character of basic science and, for that matter, the character of science. It makes for a good joke to portray the scientific community as an anarchically inclined throng of people concerned only to feather their own nests with high flux beam reactors, proton accelerators and the like. In reality, however, there is more to be said than this. Although it is accurate to say that those who work in the more abstract branches of science such as high energy physics can be confident only that success will help them to define new problems, those who work in such remote byways are often buoyed up to do so by their awareness of how much the scientific enterprise can contribute to the general understanding and well-being of society. Professor Wheeler, of whom Lord Rothschild made fun on Wednesday, chiefly on the strength of an extract from a popular science weekly, is not merely a student of the "chemistry of geometry in superspace, where neither time nor space exist" but also the man chiefly responsible for an understanding of the way in which uranium atoms can be induced to split almost exactly (but not quite) in two. And the young men and women who have in the past and will in the future be induced to become scientists are often persuaded to do so by their recognition that their craft is in the long run beneficial. There is room for argument, quite legitimately, about the balance to be struck between basic and applied research. Most probably there has been too much of the first and too little of the second. The Science Research Council has been doing its best to put things right. But it will be to discard the baby with the bath water to create in the British scientific community such a sense of gloom that nobody cares much for research as such. That is the biggest danger in Lord Rothschild's declaration.

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100 Years Ago

At the meeting of the Royal Geographical Society on Monday last, Sir Henry Rawlinson stated that the Council intended to address the Foreign Office, with a view of arranging, either directly from the Foreign Office, or through co-operation between the Foreign Office and the Society, some means of communicating with Dr. Livingstone, either by sending messengers into the interior of Africa, and offering a reward of 100 guineas to any African who will bring back a letter in Dr. Livingstone's handwriting to the sea-coast, or by organising a direct expedition, headed by some experienced and well-qualified European, who should himself penetrate to the point where Dr. Livingstone is supposed to be.

We learn from *Les Mondes* that the lamentable disagreement between M. Daubrée, the director of the mineralogical department of the Museum of Natural History at Paris, and his assistant, M. Stanislas Meunier, is now happily terminated, and that the latter is again permitted to carry on his researches at the Museum.

From Nature, **5**, 131, *December* 14, 1871

OLD WORLD

MARS

Arrival of Russians

by our Soviet Correspondent

THE safe arrival of the Soviet Mars-2 probe in an 18 h areocentric orbit on November 27, 1971, followed on December 2 by the soft landing of an instrument capsule from Mars-3, has led to self-congratulation in the Soviet press that the guidance and orientation problems which led to the failure of Mars-1 (launched November 1, 1962), and presumably Zond-2 (launched October 30, 1964), have been overcome.

Part of this success seems attributable to the use of on-board guidance systems—the orbital injection of Mars-2 was carried out without ground control, by means of an automatic device which aligned on the Sun and a star (probably Canopus). Another important factor (judging from the amount of press coverage it has obtained), the difficulty of keeping the solar batteries aligned with the Sun while simultaneously keeping the transmitting and receiving aerials pointing at Earth, has at last been resolved. (Academician A. A. Blagonravov, speaking at the Sixth Annual Meeting of the International Council of Scientific Unions' Committee on Space Research, explained that contact with Mars-1 had been lost when "a defect in the probe's orientation system resulted in a violation of the directionality of the probe's antenna to Earth".)

Less, however, has been made public about the intended experiments to be undertaken by the two probes. The TASS reports at the time of launching indicated merely that they were "to investigate the planet Mars and the neighbouring region of space and to investigate the characteristics of the solar plasma, cosmic rays and the radiation picture during the flight from Earth to Mars"

The results from the in-flight investigations are now being processed and compared with the data obtained from Cosmos satellites, Lunokhod-1 and Luna-19. Special attention has been paid to the study of the Earth's magnetic tail, and it seems (*Pravda*, December 4, 1971) that a special attempt has been made to repeat the experiments of Pioneer-7, Pioneer-8 and Mariner-4. The two Mars probes passed through the "tail region" at a distance of 20 million km (3,000 Earth radii), a distance at which Mariner-4 failed to locate traces of the geomagnetic tail. The Mars-3 readings, however, showed that for about 36 hours the distribution of charged particles with respect to velocity differed considerably from that characteristic of the solar wind—the "most probable explanation" being that at this time the probe was passing through a region of mixing of the solar wind and geomagnetic tail, and that, therefore, the tail is still observable at this distance.

Mars-3 is also carrying the French Stereo-1 experiment, designed by Drs Steinberg and Carubos of the Meudon Observatory to study the directivity of the radiation from solar bursts. This device, mounted in the solar battery unit to ensure constant solar orientation, continuously monitors the solar radiation in the metre waveband, but, by comparing each reading with the preceding one and eliminating those which show no change, it transmits data only when actually sensing a burst. By comparing these readings with those taken at Nancy and at the Moscow Institute of Terrestrial Magnetism, Ionosphere and Radio Propagation, it is hoped to be able to map the "directivity diagram" of the bursts recorded.

The investigations to be carried out in areocentric orbit are, so far, less explicit. In a *Pravda* interview (December 3, 1971) Dr M. Ya. Marov hints, however, at a programme largely based on study of the "radiative capacity" of the planet, over a wide range, from the ultraviolet down to centimetre wavelengths. Thermal mapping of the planet is to be carried out, allowing the properties of the surface to be postulated. The chemical composition of the atmosphere is to be investigated by infrared and ultraviolet, special attention being paid to any indications of traces of nitrogen and water vapour. Important questions behind the Mars programme are: What gas predominates in the upper atmosphere of Mars? What ions are in its ionosphere? Why has Mars no magnetic screen and what are the differences in the interaction of Mars and Earth with the solar plasma? Dr Marov does not, however, indicate to what extent these questions will be answered by the two current probes.

The current Mars probes, with a mass of 4,650 kg, are more than five times heavier than the ill-fated Mars-1. One would expect, therefore, a considerable increase in the experimental capacity. Yet, in the case of Mars-2, which it now seems likely is intended for orbital survey (the hammer and sickle capsule deposited on the surface shortly after orbital injection apparently was meant merely as a symbolic gesture in case of the failure of Mars-3), with the experiments being very similar to those intended for Mars-1.

Clearly as much equipment for orbital work as possible has been placed aboard Mars-2, leaving any extras, such as Stereo-1 and of course the landing capsule, to be carried by Mars-3. Although the telemetry signals from Mars-2 and the remaining orbital section of Mars-3, as monitored by Jodrell Bank, are similar but for a greater signal strength from Mars-3 (it has not so far proved possible to monitor signals from the surface), the probes do not seem to back up each other but are complementary. This is perhaps regrettable, especially in view of the reported failure of the cameras aboard the landing capsule, but it may not only be due to a tendency of the Soviet space programme planners to avoid duplication; the question may, ultimately, be one of weight.

It has been stressed several times in the Soviet press that the new on-board computer and guidance system makes great use of micro-miniaturization, and the very emphasis on this fact, plus the apparently similar or diminished experimental capacity of Mars-2 in comparison to Mars-1, does suggest that a relatively large proportion of the weight increase of the current probe has been expended in bringing them into orbit, leaving too little available for the duplication of even the most important experiments.

PHARMACEUTICAL INDUSTRY

Beecham to Win?

IF the Glaxo shareholders agree to the recently announced bid of £290 million by Beecham for their company and if the matter is not referred to the Monopolies Commission, it seems likely that the new year will see the creation of a pharmaceutical concern which will dominate the British market and rank about tenth or eleventh in the world. But what are the factors that determine whether Glaxo is ripe for a takeover?

Certainly the announcement last month that Glaxo had suffered its first drop in profits for more than ten years is an indication that all is not well. But in the pharmaceutical industry, where the failure rate among new compounds is astonishingly high, success is often as much a matter of luck as of expenditure on research and development. And the sixteen year protection given by patents is nowadays effectively reduced to twelve years or so because of the extensive toxicological and clinical tests that are required before new drugs can be marketed.

Glaxo and Beecham are in many ways quite similar—their sales are £173 million and £182 million a year respectively and they each spend about £5 million a year on research and development. Most of the Beecham research is done at laboratories at Brockham Park, Surrey, where 25 per cent of the staff of 400 are graduates.

It was in these laboratories that the first semi-synthetic penicillins, which have formed the backbone of Beecham's ethical drug sales, were developed in the late 1950s. There are two other smaller Beecham research laboratories —at Walton Oaks, Surrey, and Harlow, Essex. The first of these was part of the research organization of Vitamins Ltd, a company bought by Beecham in 1967, and the second was opened by Beecham itself in 1969. Most of Beecham's nutritional research is carried out at Walton Oaks and the Harlow laboratory is responsible for the synthesis and evaluation of compounds other than antibiotics.

Research at Glaxo is also conducted at three chief research centres, two of which were inherited as a result of the purchase of Allen and Hanburys and BDH Pharmaceuticals. Most of the Glaxo research is centred on Glaxo Research Ltd, Greenford, and some is also carried out by Glaxo subsidiaries in India and Italy. The planned growth of expenditure by Glaxo on research and development was spelled out by Sir Alan Wilson in the company's annual report for 1969-70. He then announced that the research and development budget would double by about 1975. Extensions to the research laboratories of Glaxo and those of Allen and Hanburys are also in hand and are expected to be completed by the middle of 1972 at a cost of £5 million.

It may be significant that about 65 per cent of Beecham's sales are of non-ethical products whereas the corresponding figure for Glaxo is 45 per cent. Glaxo has yet to show that it will reap just rewards from the £55 million which it has invested in drug manufacturing plant since 1969.

SPACE

Ionosphere Probe

Earlier this week the latest in the Ariel series of British satellites was being prepared for launch from the Western Test Range in California on December 11. The satellite is a repetition of the previous satellite in the series, Ariel 3, but with many significant modifications and improvements. An experiment from Professor L. A. Frank's group at the University of Iowa has been added to the previous portfolio of experiments from Jodrell Bank (Professor F. G. Smith), the University of Sheffield (Professor T. R. Kaiser), the University of Birmingham (Professor J. Sayers) and the Radio and Space Research Station of the SRC (Mr R. Dalziel). An experiment from the Meteorological Office on Ariel 3 has been omitted this time.

As luck would have it, a fault connected with the EHT monitor in the guest experiment from Iowa has been responsible for a postponement from the original launch date in November, since when Professor Frank's group has been working to ensure that the fault does not reflect a more serious problem within their experiment.

Ariel 4 was designed to provide an integrated series of experiments to study the interactions among plasmas, particles and waves in the upper ionosphere. To this end it will be placed in a 550 km orbit inclined at 83° to the equator to ensure world-wide coverage. Like its predecessor, Ariel 4 will rely on tape recording to store information until the satellite passes over a ground station. Although the tape recorder on Ariel 3 worked perfectly for 9-10 months (surpassing the previous record of 3 months for the durability of a tape recorder in space), the experimenters are aware that the recorder is the weak link in the system. Ariel 4 therefore carries two tape recorders to postpone the time when the experimenters will have only real time data available to them.

The original design has also been modified to include safeguards against interaction between the aerials of the Birmingham and Jodrell Bank experiments, which on Ariel 3 resulted in signals from the Birmingham experiment being picked up by the Jodrell Bank experiment and interfering with the collection of data.

By obtaining simultaneous observations of various aspects of the conditions in the upper ionosphere, Ariel 4 should throw some additional light on the physical processes involved in the ionosphere and magnetosphere. The Iowa experiment will examine protons and electrons between 5 eV and 50 keV, the Jodrell Bank experiment will look for radio waves which it is believed may be generated by streams of charged particles interacting with the magnetosphere and ionosphere through the Čerenkov effect, the Sheffield experiment will record ELF and VLF emissions related to the flux of charged particles as well as emissions originating from stations on the ground (which are of course influenced by the conditions in the ionosphere) while the Birmingham experiment will provide the measurements of local electron temperature and density which are essential to an interpretation of the other data. The Radio and Space Research Station is involved in both the Jodrell Bank and Sheffield experiments.

SPACE

Per Ardua ad Terminum

from *La Recherche*

No complete technical explanation for the failure of Sunday's Diamant B booster rocket seems likely in the immediate future. The Diamant B has been used successfully on three previous occasions, but a strong vibrational "pogo effect" was noticed on each occasion and, in spite of repeated efforts to eliminate this, it proved impossible to do so. There were also defects in the Diamant B's electronic systems which helped delay this last launching, originally planned for December 2. Yet neither of these shortcomings appears to be responsible for Sunday's abortive mission.

Psychologically, the consequence of this episode is one of virtual disaster at the Centre National d'Etudes Spatiales (CNES) where the government's budgetary austerity had already introduced a note of uncertainty into the future of the French space programme. Politically, the failure of this last launching could not be more inopportune. The French government had envisaged, for some time now, imposing financial limitations on France's role in the space effort. A study group was to have examined, in January, the possibility of reducing expenses at the Guyana base, and if need be even closing down the base for several

Royal Society

Professor A. L. Hodgkin was re-elected president of the Royal Society at the anniversary meeting of the society held last week. The other officers re-elected were Sir Frederick Bawden, Rothamsted Experimental Station, treasurer; Sir Bernard Katz, University of London, biological secretary; and Sir Harrie Massey, University of London, physical secretary. Professor K. C. Dunham, University of Durham, was elected foreign secretary.

The full council of the Royal Society for this year will consist of the officers, together with Professor E. J. W. Barrington, University of Nottingham; Professor J. W. S. Cassels, University of Cambridge; Professor A. R. Collar, University of Bristol; Dr H. M. Finniston, British Steel Corporation; Professor L. Fowden, University of London; Professor R. A. Gregory, University of Liverpool; Professor H. Harris, University of Oxford; Professor A. W. Johnson, University of Sussex; Professor R. V. Jones, University of Aberdeen; Professor R. A. Morton, University of Liverpool; Professor C. W. Oatley, University of Cambridge; Professor D. C. Phillips, University of Oxford; Mr J. D. Rose, Imperial Chemical Industries Ltd; Professor P. A. Sheppard, University of London; Professor K. Stewartson, University of London; and Professor D. H. Whiffen, University of Newcastle upon Tyne.

months each year. Next spring, the French government will be faced with the choice of continuing to build the Diamant B booster or giving up the Diamant B and buying the American Scout. CNES's future was not very bright to begin with. Since last Sunday, it is gloomier still.

AUSTRALIA

CSIRO Restrained

THE Australian Commonwealth Scientific and Industrial Research Organization spent $A60.2 million in 1970–71, about 60 per cent of Australia's public expenditure on research and development. Although the annual report (CSIRO, Melbourne, 1971) reveals that the organization's budget was $A8.4 million higher in 1970–71 than in the previous year, CSIRO has clearly been feeling the effects of the federal government's restrictions on public expenditure that were imposed in February this year.

The organization's building programme, for example, had to be trimmed from the $A2.8 million originally approved to $A1.1 million but, in spite of the cuts, work commenced on the site of the new National Standards Laboratory in Sydney and on the construction of several other laboratories. The chief project completed during the year was the new CSIRO head office building in Canberra which cost $A1.5 million and was funded separately by the federal government.

Although 80 per cent of the income of CSIRO during 1970–71 was provided by the federal government, most of the remainder came from levies on the produce of Australia's agricultural industries—wool, meat, wheat, dairying and tobacco—which are matched dollar for dollar by the federal government. Some of the CSIRO work of particular interest to the wool industry may soon have to be curtailed because of reduced returns from the sale of wool, and the report also says that "similar difficulties may be expected to arise with others of the agricultural industry trust funds".

As well as bread and butter research and development in such fields as chemistry and physics, some parts of the organization are also engaged in work related to the needs of the Australian mineral industry. $A3.4 million was spent on the processing and use of mineral products in 1970–71, for example, and other related research includes efforts to improve the techniques of mineral exploration and to understand more fully the disposition and mode of formation of metal ores—particularly nickel sulphide, the copper-lead-zinc ores and the ores of tin.

Electron Accelerator

THE meeting of the European Committee on Future Accelerators (ECFA) in Geneva last week (see *Nature*, **234**, 242; 1971) took no decision to set up a working party on the feasibility of a European Electron Accelerator. Professor A. Ashmore, director of Daresbury Nuclear Physics Laboratory, said that the committee was not in favour of starting any new project on the scale of the 300 GeV machine until that accelerator is completed. The meeting did, however, discuss the proposal in general terms and Professor Ashmore thinks it possible that a working party will be set up at the next meeting of ECFA in about six months time.

EQUAL PAY

No Lib Yet

THE letter from Professor David Layzer and his twenty-two co-signatories (see page 369) has raised the question whether *Nature* alone lacks a "non-discriminatory advertising code" and the probability that other newspapers and journals are refusing to publish advertisements which state that women are to be paid less than men. Telephone enquiries this week suggest, however, that those bastions of the British Empire (as was), the *Daily Telegraph* and *The Times*, do not refuse to publish advertisements which discriminate against women. Both declared themselves quite happy to publish anything that anyone is prepared to pay for, provided it is within the letter of the law—although *The Times* did admit to having had trouble over an advertisement for a Scottish lawyer when the intention had been to recruit a lawyer expert in Scottish law.

In the United States some newspapers have had to close their women's appointments column. Have British papers received any complaints? The *Daily Telegraph* says no, *The Times* says yes—a couple—but as the advertising manager said in another context, *The Times* is read by some of the best brains and the biggest cranks in the world.

On the subject of pay discrimination the Canadian High Commission said this week that its women scientists are paid the same as its men. At South Africa House they said that in industry women's pay is not always the same as that of men, but that in the Civil Service it is—"Well, there might be a few bob difference".

The president of the Women's Engineering Society, Miss Peggy Hodges, said that there is a large area in British industry where pay is nominally equal, but where equal opportunity is quite another matter; women have to be better than men to hold down the same job, she said. What did she know of the position in America? She said that at the Third International Conference of Women Engineers and Scientists in Turin last September, she had the impression that in the United States also no more than lip service is paid to equal pay and that there certainly wasn't equal opportunity and she got the impression that "the position was, if anything, slightly worse". Oh dear. And when David Layzer, Randy Levine, Martha Schwink and company can spare a glance at their own problems and away from their suffering cousins 10,000 miles away in Sydney, perhaps they might read an article in *Science* (**174**, 270; 1971) which suggests that there might be a few battles over equal opportunity still to be fought on the good soil of the homeland before they venture so far abroad.

However, to keep their fighting pecker up with a sniff of victory, we did also ring the Australian Atomic Energy Adviser in London who placed the advertisement. Had anyone ever refused to carry one of his advertisements?—no. Was there much in the way of protest about unequal pay in Australia? Well, quite a bit, he said. Could he foresee a time when women in Australia's Commonwealth Civil Service would be paid the same? Mr Fry said he wouldn't like to hazard a guess. In half an hour he rang back. Women scientists in the Australian Civil Service are to receive equal pay from January 1 next year. One more down, a few more to go.

TECHNOLOGY

A White-hot Haze

THAT the understanding and practice of technology must play a larger part in school timetables was the basic assumption behind a one day conference at the Open University last week on introducing technology into the school curriculum. It was also the only area of clear agreement.

The conference, sponsored by the Guinness Awards Scheme, was partly held to gauge reaction to a proposed conversion course in technology for teachers that Mr Geoffrey Holister, Professor of Technology at the Open University, hopes will be approved in principle by the university senate at its February meeting. The details of the course have yet to be worked out, but its aims are to provide teachers with an awareness of technology and its social implications, and an ability to solve problems put before them. It would also help teachers to pass on these abilities to their pupils.

What all this means in practice is far from clear—what people mean by technology varies considerably from applied science to a rather diffuse sort of sociology. The forty participants, from universities, colleges of education, the Schools Council and the research councils, also disagreed about whether technology should be taught for its own sake—with all the disciplines that embraces—or whether teachers in all subjects upon which technology impinges should be made more aware of technological implications and should then cooperate to encourage children to tackle suitable projects. This second view that technology should be taught by a change of attitude rather than a change of subject was the more popular at the conference and was clearly seen by some as part of a more broadly based approach to education as a whole, so that subjects that interrelate are taught together, in the humanities as well as the sciences.

The Open University's proposed course was cheered on, but if technology is to be introduced into schools by retraining teachers some of the participants were clearly apprehensive about the amounts of equipment that will be needed. Professor Holister suggested the provision of kits of the type to be used for the Open University technology course might help. But others argued that kits are limiting and tend to become an end in themselves as Professor Carter of Salford University claimed the Nuffield Science O- and A-level kits have become. Should technology in schools be the solving on paper of problems with as many social and economic aspects as technical ones, or should it be the understanding and use of computers and other technical equipment? Either way there were warnings that technology in schools will cost money. Those involved in A-level courses in engineering claim that a teacher cannot handle classes bigger than twelve if open ended problems are to be studied like the technical, social and economic problems of high rise flats.

At present technology in schools is encouraged largely by the Schools Council's Project Technology — which began life in 1967 and which provides teaching material to 1,000 schools. This material is soon to be published in book form. After Project Technology's demise in August 1972, there will be little active encouragement of school technology other than by a number of bodies that intend to carry on Project Technology's work, although, to date, they have more enthusiasm than money. There are also fourteen technology advisers to local education authorities and four (there are more planned) local science and technology centres which provide schools with facilities. But with 163 local education authorities in England and Wales alone, these are only a drop in the ocean, unless something like teacher retraining is undertaken.

What emerged from the conference was a rather hazy conviction that more must be done to introduce technology into schools. But what that technology in fact is, and how it should be taught, have yet to be defined.

ANTI-VIVISECTION

Cells do not Suffer

THE Anti-vivisection Society's bandwagon rolls on with the release of a film last week to promote opposition to experiments on living animals and a campaign for a national centre to investigate methods of research without vivisection. When the society was formed in 1875, 300 experiments a year were carried out on live animals; last year the figure was just over 5½ million. The society opposes in principle all painful experiments on live animals even where man benefits directly, but appreciates that these cannot be stopped overnight. Its first object is therefore to change the law so that no animal may be subjected to vivisection if there are alternative methods—such as cell culture—available.

The society claims that support for its cause is growing. One hundred and thirty Members of Parliament are said to have pledged their support, and the society claims that a letter sent to the 14,000 researchers licensed by the Home Office to work on living animals produced 1,000 replies supporting in principle the research centre they propose. They also admit to receiving 1,000 letters against their proposal.

Asked to put a figure on the cost of such a centre, the society estimates that the first step in such a scheme—the collation of all known material on research methods other than vivisection—would cost £0.5 million, but that the actual cost of building the centre is anybody's guess.

Mr Richard Body, MP, one of the society's vice-presidents, claims that Britain is "far behind countries such as Turkey, Yugoslavia and even Russia" in concentrating on cell and tissue culture rather than vivisection, although in fact the legal controls in Britain are among the stiffest in the world. Every laboratory has to be licensed by the Home Office (there are about 600) before it can experiment on animals, and every researcher within a laboratory has to have a personal licence. Whether the anti-vivisectionists will ever command enough public and parliamentary opinion to achieve their aims remains to be seen, but the adoption of a resolution by the Consultative Assembly of the Council of Europe last January recommending a study of alternative methods to vivisection may lend some support to Mr Body's claim that the movement is "rapidly gaining ground".

EUROPEAN LABORATORY

Still Waiting

THE absence through ill health of Professor G. Puppi, chairman of the Esro council, from the council meeting held in Paris on November 23 and 24, caused the expected press conference to be cancelled and probably saved Esro a great deal of embarrassment. The Esro council continued its meeting this week and it is expected that an announcement about the future of the European Space Research Institute (Esrin) will be made today (December 10).

The meeting held two weeks ago was notable for the measure of disagreement among the delegates on the future course of Esro. In particular, no decision was reached on the vexed question of whether Esro is to continue supporting Esrin and the Italian plan for the future of the laboratory (see *Nature*, **234**, 165; 1971) was not discussed—ostensibly because of the absence of Professor Puppi who has been personally conducting negotiations with the interested parties. In spite of there being no detailed discussion on the future of Esrin, the Italian delegation confirmed reports that they were determined to keep some Esro activity at Esrin—according to the plan that was discussed this week, the Italian delegation suggested that the Centro Nazionale delle Ricerche (CNR) contribute $1.7 million towards the running costs of Esrin and Esro the remainder—which would amount to $1.0 million.

The original objection to the continued existence of Esrin within the Esro framework was that it carried out research that was not compatible with the present aims of the organization. It was therefore surprising at the meeting on November 23 and 24 that both the German and Dutch delegations made statements to the effect that the continued support of Esrin in its present form amounted to a financial problem for the organization.

The threat of the Italian withdrawal from Esro hung over the meeting (see *Nature*, **234**, 3; 1971) and although it was agreed at the Esro council meeting held in July that Germany, France, Italy and Britain would continue to support the applications satellite programme, the Italians now mentioned that they were reserving their support—probably until a decision was made on the future of Esrin. As a result of the Italian change of heart the Esro council this week reconsidered the future plan for Esro that was mapped out in July.

EDUCATION

Craft Training Examined

A MUCH needed inquiry into the relevance of school teaching in industrial training is to be undertaken in a four year research project at the Centre for Science Education, Chelsea College of Science and Technology. The project, financed by a grant of £45,580 provided jointly by the Engineering Industry Training Board and the Leverhulme Trust, is to be directed by Dr Erica Glynn, who also directed the one year feasibility study that led up to the formation of the present project.

One of the objectives is to see how the performance of industrial trainees depends on training at school. In particular there will be an attempt to relate the performance of trainees who have studied science by an innovative scheme —for example the Nuffield scheme—to those who have learnt their science in a more conventional way. A further objective is to obtain information on what training best suits school leavers of differing educational backgrounds.

Perhaps the most important by-product of the inquiry will be to forge an association between school and industry and to correlate teaching methods and training. It is this aspect of the work that has attracted the support of the Engineering Industry Board, which hopes that the inquiry will lead to a more efficient and practical training scheme for industrial trainees.

The impetus for the new study comes not only from the one year feasibility study, but from a similar study of the training of craft apprentices started in 1966 at the Perkins Engines company which was also supported by the Engineering Industry Training Board. This report, published earlier this year, suggests that the choice of methods open to the craft instructors is considerably wider than previously assumed and that "guided discovery learning" is particularly effective.

The study team plans to concentrate its investigations in selected areas where the project team and people in education and industry will cooperate to define the problems to be studied to minimize any misunderstanding.

The research programme will be in three phases:

- Local in-depth studies to develop tests and questionnaires.
- The testing of detailed hypotheses, making use of information obtained in the first stage of the investigation, by following the performance of potential trainees from their last year in school through their first year of training.
- Analysis and evaluation with continuing study of the performance of some craft trainees into their second year of training.

SCIENCE POLICY

Lord Rothschild Says It Again

THE Royal Society of Arts, more fully known as the Royal Society for the Encouragement of Arts, Manufactures and Commerce, heard from Lord Rothschild himself, on Wednesday this week, of the philosophy underlying his proposals for the reorganization of the British government's interests in civil research in Britain and in particular for the redefinition of the relationship between the research councils and government departments. Quite apart from the claim on public attention which his report (see *Nature*, **234**, 169; 1971) has established, there is also a chance that Lord Rothschild will become the most amusing civil servant to work for the present government.

The classification of research attracted a good deal of his irony. He complained of those "ex-research workers who are the high priests of the cult" who have kept the "taxonomic bandwagon" rolling and in particular of the concept of "pure basic research". But what about research on the nature of the immaterial world? Is that impure? "One had better ask Zuckerman" for, as Lord Rothschild pointed out, Lord Zuckerman's co-author of the Gibbs-Zuckerman report in 1961 "is no longer with us". On that classification, there was also "objective basic research" which is relevant to known objectives in technology, applied project research with a practical goal, applied operational research which is the improvement of the devices which exist already, and development, to bridge the gap between research and production. "One wonders for whom this elaborate taxonomy was necessary and to whom it is useful."

The taxonomic point is important in Lord Rothschild's argument because it is the starting point for his principal conclusion and on Wednesday he complained of the taxonomy put forward by Sir Frederick Dainton's committee, with its concepts of basic research, strategic research and technical research. In practice, he said, it is not possible to make distinctions like these with any accuracy.

Basic research, however, does have a place in Lord Rothschild's scheme of things. Basic research "is done solely to increase knowledge". Researchers must be competent but need not justify their activities "on the grounds that they may help mankind". It may happen that basic research turns out to have practical value, but that is not essential. Society will back good people "provided what they want is not too obviously anti-social. Whether society will go on backing every Tom, Dick and Harry who is inquisitive but not too gifted, and let them do what they like at public expense for three or so years at a university after graduation, is a matter on which we would do well to ponder. We do not want to have too many lift attendants, taxi drivers or uniformed commissionaires with PhDs in the natural sciences . . .". The strength of Lord Rothschild's taxonomy is its simplicity—there are only two categories, the second of which he calls applied research and development. "It is indistinguishable from pure research as regards how it is done. The distinction lies in why it is done and who wants it done." Applied research needs an objective—putting men on the Moon, providing blind people with artificial eyes, making cars less noisy and noxious, reducing collisions in the English Channel, providing three-dimensional colour television screens. Indeed, the choice of technical objectives is so great that, in Lord Rothschild's view, it is no longer true—if it has ever been true—that what "can be done will be done". On the contrary, "we have, in fact, got to the end of the road, where the man who determines the objective for which applied research is necessary has got to justify the objective to a form of shareholder, whether it be the electorate and their representatives in Parliament or that somewhat elusive and inarticulate person, the shareholder in a company."

In Lord Rothschild's view, outside scrutiny is also required for basic research projects. Some kind of basic research "might have dangerous consequences or side effects" and society could not be expected indiscriminately to acquiesce in the conduct of work like this and the dissemination of the results. ". . . Sooner or later we shall have to control those types of basic research whose indiscriminate exploitation would or might be harmful to society. Interference with the liberty of the subject? Yes, but is there ever, in reality, absolute liberty? I think not."

Lord Rothschild is not, from what he said on Wednesday this week, an instinctive supporter of "big research". The proton accelerator being built near Chicago on 6,800 acres of prairie, and already equipped with three artificial lakes for fishermen, two herds of buffalo and an office in Chicago for the recruitment of black workers, had already cost £100 million and was no doubt a forerunner for an instrument that would cost ten or a hundred times as much. Such a "gadget . . . with or without the lakes and buffaloes" was outside the British purse, "but in our own modest way we have similar intentions". Lord Rothschild went on to refer to the proposal that the Science Research Council should finance a high flux beam reactor at a cost of £22 million and he wanted "the scientific establishment" to ask whether it might not be better to spend the money on Titian's Death of Actaeon (which would still leave room for another nine equally expensive paintings), twenty miles of motorway, four hospitals, 300 adventure playgrounds, four prisons, 200,000 television sets, two Jumbo jets or 4,500 houses.

How should people decide what projects in applied research should be supported? Quality of research and individual creativity are no less important than elsewhere but there are also questions to be asked of economists, those who value clean air and clean country and even those who worry about law and order. "These deep and fundamental national questions cannot be decided by scientists alone" and in this sense Britain shares with other nations an anachronism. He was not seeking a regime in which scientists would be told meticulously what to do but he did protest against the "pedestalization of science" and the way in which the admiration of the British for pure science spilled over into the making of decisions on applied science. "Have we not got 4.6 Nobel prizewinners per ten million of our people in comparison with America's 3.3?" Scientists might have a part to play in studying problems such as urban conglomeration, agricultural needs and drug addiction, just as do other people—sociologists, engineers, lawyers, economists, accountants, mathematicians and administrators. Unhappliy, in Lord Rothschild's view, the government was still too wedded to the idea that in circumstances like this it was necessary only to find good scientists "and let them get on with the job". He blamed not so much the people themselves as their willingness to invoke the outmoded Haldane principle, with its justification of scientific freedom or, rather, *laissez faire*.

Lord Rothschild complained that one of the consequences of the Haldane principle had been to polarize society into scientists and the rest, with detrimental effects on government research and development and with the result that there had emerged autonomous bodies, the research councils, which were accountable to Parliament but "not accountable to anybody else in spite of their names which include such bizarre words as agricultural, medical and natural environment. Is it not strange that though the taxpayer pays for these bodies, he has no say in what they do?"

Lord Rothschild went on to say that "we scientists are neither black, selfish, thoughtless and unpatriotic; nor are we white, selfless, unthoughtful patriots. Like virtually everyone else, we are grey curates' eggs." And scientists are conservative and were hanging on to the Haldane principle, as interpreted, without recognizing how much damage it had done in polarizing society and the civil service.

What is to be done? Lord Rothschild was optimistic about the problems of the civil service, which will be solved "during the next five or so years". Nor is he worried about basic research, an activity in its own right even if it does consume between 13 and 17 per cent of the British government's expenditure on research. But he did ask that applied research should be linked with practical objectives, that research workers should not be solely responsible for formulating these objectives nor even for deciding whether "the objective requires research for its achievement. He should not decide that the research should be done, assuming it is necessary. He should not decide when to stop. Nor should he decide to change the objective in midstream, however desirable it may seem to him to do so." Rather, it is for scientists to do the research and to help out when they can.

Scientific Administrators

Lord Rothschild said this week that within five years there would be a free interchange of scientists and administrators within the civil service. The present reluctance to have such interchange is, according to Lord Rothschild, not due to administrative, financial or geographical difficulties but because a belief pervades the civil service that administrators cannot play an important role in scientific policy making and that scientists make bad administrators. The truth, according to Lord Rothschild, lies somewhere in between.

Mr William McCall, general secretary of the Institution of Professional Civil Servants, who has been agitating for such an interchange for some time, said this week that he was delighted with this aspect of Lord Rothschild's lecture. Mr McCall added that the foundations of a better arrangement for interchange will be laid soon and that he was determined that the system should be in full operation within five years.

This is where the doctrine of the customer and the contractor comes in. Lord Rothschild has no strong opinion, to tell from his lecture on Wednesday, about the kinds of basic research that should be carried out. "What, however, I do object to is virtually all medical, agricultural and environmental research being controlled autonomously by scientists and to a lesser extent mathematicians and engineers, with concomitant downgrading of the research commissioned by government departments and, with a few exceptions such as Bell Telephone Laboratories, by industry. We must, I believe, oppose the deliberate creation and nurture of this kind of scientific elite—the autonomous haves and the departmental or industrial have-nots."

By his own admission, Lord Rothschild seems well aware that his philosophy "is anathema to very many scientists, particularly of course to some of those intimately connected with our research council system". Haldane has been beatified by the scientific establishment and Lord Rothschild was particularly scornful, in his address on Wednesday, of Sir Harold Himsworth's defence of the research council system in his book *The Development and Organisation of Scientific Knowledge* (Heinemann, 1970). Is it possible that scientists are so corrupt that they will cook the books when working for government departments? Can ministers in the 1970s actually suppress facts? Is it sensible to fear that venality in government departments can survive in the face of honesty from abroad?

But what is it all for? Lord Rothschild's complaint is that the scientific community is clinging to outdated concepts. He considers that there is no such thing as science policy but that it is important to develop policies on pollution, ocean resources, food supplies and so on. But "science as a whole is not an activity to be carried on in isolation. It must be part of society's integrated effort to make the world a better place." And it is for "democratic society itself and its elected representatives" to give scientists their marching orders.

NEW WORLD

NATIONAL SCIENCE FOUNDATION

Stever Confirmed

by our Washington Correspondent

AFTER twenty minutes of gentle and rambling questioning of Dr H. Guyford Stever last week, the Senate Committee on Labour and Public Welfare agreed, as everybody expected, that Dr Stever is suitably qualified to be the next director of the National Science Foundation. The Senate later went through the formality of confirming his nomination, and Dr Stever is now all set to take over from William D. McElroy who leaves the NSF in February next year to become chancellor of the University of California at San Diego.

Last week's gentle grilling—if a series of congratulations and a dialogue in which committee members had most of the say can be so described—elicited few surprises about Dr Stever's policies for the NSF. Asked by Senator Edward M. Kennedy about his attitude to the RANN (Research Applied to National Needs) programme, for example, Dr Stever replied that the programme "is a very important programme to the NSF" since it helps to turn out from the universities more students who are aware of society's problems and needs. The programme also happens to be one on which the NSF is particularly keen, in spite of congressional disfavour last year, and Dr Stever's background as an engineer should help him in his arguments before Congress next year when he asks for more money for the RANN programme.

As for institutional support grants, which last year were severely reduced in the Administration's budget requests to Congress, reinstated by the authorizations committees but partially withheld by the Office of Management and Budget, Dr Stever seemed to be in two minds. As a university president who has been particularly successful in getting NSF institutional support in the past, Dr Stever considers such grants to be "very valuable", but the director-elect, perhaps toeing the Administration line, pointed out that when it comes to apportioning scarce resources, some areas are bound to suffer, the clear inference being that cutting institutional support may be less damaging than paring funds for particular areas of research—a drop in funds for high energy physics has already "contributed to unemployment", Dr Stever said. Nevertheless, if Dr Stever is put in the position of arguing for a cut in institutional support grants for the 1973 budget, somebody is bound to point to his testimony before the House Subcommittee on Science, Research and Development in 1969, when he thoroughly endorsed institutional support as a particularly valuable instrument for stimulating basic research in the universities.

Dr H. Guyford Stever, the next director of the National Science Foundation

That Dr Stever would be acceptable to the Administration and to Congress has scarcely been in doubt since the National Science Board recommended his name to the White House nearly three months ago. His background as a scientist and engineer, administrator and veteran of the Washington science advisory network (see *Nature*, **234**, 122; 1971) won him points with Congress and the White House was also impressed by the fact that he is a Republican who is unlikely to be at odds with the rest of the Administration on major policy issues. Dr Stever's political background certainly ensured that there would be no repeat of the 1969 performance when Franklin Long of Cornell University had his nomination to the NSF withdrawn by the White House because of his opposition to the ABM system.

ASTRONOMY

New Face for Arecibo

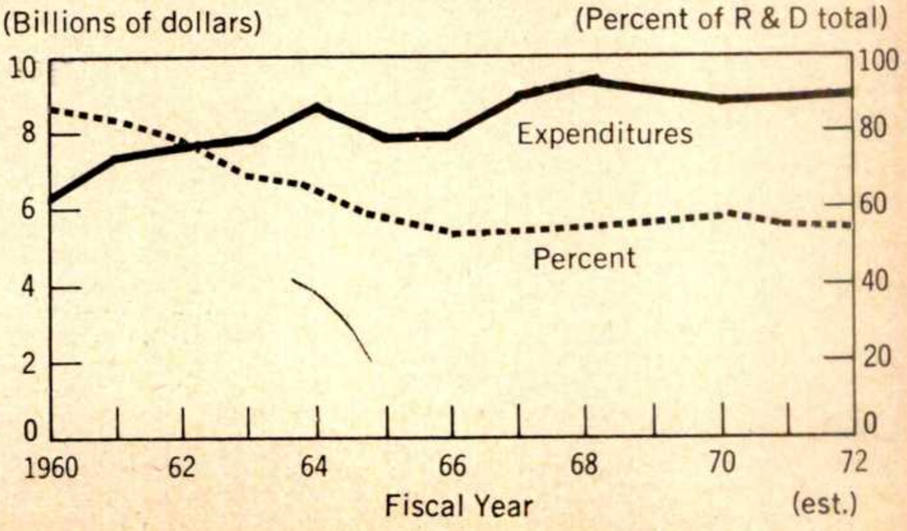
by our Washington Correspondent

A CONTRACT has at last been awarded for resurfacing the 1,000 foot radio antenna at Arecibo in Puerto Rico. The work, which will cost about $3.76 million, will take about two and a half years to complete, and should improve considerably the sensitivity of the telescope—allowing detection of about twenty times more radio sources than the presently known 5,000—and enable it to be operated at wavelengths as short as 6 cm, compared with the present minimum operating wavelength of 50 cm.

The chief objective of the work is to improve the accuracy of the surface of the telescope by replacing the present wire mesh with perforated aluminium panels—37,000 panels will cover the 18.5 acre surface of the antenna. To achieve the desired operating performance, the radius of the sphere must be accurate to within 3.2 mm at each point, compared to the present surface accuracy of about 1.5 cm, and the firm that has been awarded the contract, LTV Electrosystems Inc, of Dallas, Texas, estimates that the alterations will add some 100,000 pounds to the weight of the surface.

One of the terms of the contract is that the work should not be allowed to interrupt research with the telescope, and Mr Robert Matyas, Director of the Department of Construction at Cornell University, who is in charge of the operations, said last week that he is confident that any undue disturbance can be avoided since the resurfacing would be carried out on one area at a time.

Federal Research and Development Expenditures



ETHICS

Another Commission

by our Washington Correspondent

THE standard way to deal with any vexed problem is to appoint a committee to chew over the issue in the hope that it will come up with a workable solution. The social, ethical and legal implications of advances in biochemical research are, it seems, no exceptions to this general rule, for the Senate last week agreed to appoint a full-scale commission to take a hard look at the ethical problems associated with organ transplants, abortion, prenatal diagnosis of genetic defects, genetic engineering and a host of other problems now troubling some members of the medical and scientific community. If the commission does see the light of day—companion legislation is bogged down in committee in the House of Representatives—it will rightly be based on the assumption that such issues transcend the expertise of health scientists and, as the Senate Committee on Labor and Public Welfare says in its report on the legislation, "We can no longer ask them to grapple with these issues alone".

The legislation designed to set up the commission was reported out of the Labor and Public Health Committee early last week, and approved by the Senate with little discussion four days later. It calls for the setting up of a fifteen-member commission appointed by the President from the fields of medicine, law, theology, biological science, social science, philosophy, humanities, health administration, government and public affairs. It is intended that the commission would deliberate for two years, at the end of which it would submit a report to Congress and the President of its findings and recommendations.

Among the duties with which the commission will be charged are to analyse and evaluate "scientific and technological advances in the biological sciences, past, current and projected, and then to assess the implications of such advances for individuals and for society". An equally important part of the commission's work would be to analyse public understanding of such issues through the use of seminars and public hearings, and to evaluate public attitudes to biomedical research. The legislation authorizes an expenditure of up to $1 million for each of the two years for the commission to perform this Herculean task.

One day of hearings on the legislation, held early in November, elicited considerable support for the idea from members of the biomedical community, although almost without exception, the witnesses drew attention to the complexity of the task facing such a commission. Dr Abram Chayes of Harvard Law School, for example, suggested that the commission is needed because it would have the time and resources that have been missing from previous attempts to view the problems, and Dr John Najarian of the University of Minnesota said that the commission would do valuable work if it came up with guidelines on, for example, what is considered to be a definition of death.

A note of warning was, however, sounded by reports and testimony from members of government agencies. Dr DuVal, Assistant Secretary for Health and Scientific Affairs of the Department of Health, Education and Welfare, said, for example, that "the issues are so complex and the underlying currents of change moving so swiftly that in our view no attempt to describe this particular healthscape, at what would have to be a given moment of time, could be definitive for long". But the committee does not agree, for it is looking to the commission to recommend procedures to grapple with the important problems on a continuing basis. Perhaps the most valuable accomplishment of such a commission, however, would be to open up to public discussion important ethical and social issues that have in the past been unnecessarily private.

PREDATOR CONTROL

How to Kill Coyotes

by our Washington Correspondent

LAST year, 74,000 coyotes were killed as a result of federally financed poisoning programmes, which have been under the control of the Department of Agriculture for the past 40 years. But, according to Senator Gale W. McGee, there has never been a census taken of the number of coyotes in the United States, and "while it appears we have been attacking the problem with vigour and persistence, we have not made any attempt whatsoever to determine and define the scope of the problem itself". This and other aspects of predator control in the United States will, however, be the subject of an inquiry next week by Senator McGee's Agriculture Environmental and Consumer Protection Subcommittee of the Senate Appropriations Committee.

For many years, it has been the practice of predator control programmes to kill predators whenever and wherever they appear, with poisoning usually the first line of attack. The effects of such policies on non-target species are too numerous to mention, but of particular concern are episodes such as the killing of several dozen eagles in Wyoming earlier this year during an unauthorized control programme.

Another aspect of the problem which Senator McGee hopes to look at during his hearings is the scope of the damage that is done each year to livestock by predators. The Department of Agriculture, for example, estimates that in 1970 predators accounted for the loss of some 130,000 sheep in Wyoming, but it is not clear how that estimate was derived. Without at least any attempt to determine the scope of the problem, no realistic policies can be formulated, and the Department of Agriculture will clearly have to defend its frontier tactics of simply killing everything in sight without taking stock of the situation.

Short Notes

DDT in the Oceans

NEARLY 20 million tons of DDT have been manufactured in the world since 1944, of which as much as 25 per cent may have been transferred to the sea. About 0.1 per cent of all the DDT ever produced, or 20,000 tons, resides in the marine biota. So estimates a panel of the National Research Council in a report published last month (*Chlorinated Hydrocarbons in the Marine Environment*. Panel on Monitoring Persistent Pesticides in the Marine Environment. NRC, Washington, 44 pp.).

Research on Research

NOT merely is it possible to sponsor research on transportation but, as the Science Council of Canada has shown in its Special Study No. 17, now published, it is possible to sponsor research on research on transportation. The first volume, mercifully short, of this three-volume study, says that twenty man-months of professional effort "cannot pretend to have done more than scratch the surface". Even so, the document does play a good deal with numbers, pointing out that research on transportation, equipment as well as distance, amounts to only $40 million a year, rather less than 0.5 per cent of total expenditure on transportation as such. Worse still, most professional effort goes on such things as air transport. The document pleads that there should be a fuller appreciation of the need for a systems approach in the study, the design and the operation of transport systems—that industry should be regarded as part of the system of research, that there should be less chauvinism and more international collaboration on good works such as the development of new methods of transport.

NEWS AND VIEWS

Politics as Applied Mathematics

THERE is very little chance that politics, variously known as the art of the possible and the art of the impossible, will become an entirely rational process, but it is important not merely for politicians and mathematicians but for ordinary electors that a great deal has been done to formulate in mathematical language some of the problems with which politicians are concerned. In the past year or so, mathematical models have been constructed for such things as the economic systems of nation states, the relationship between industrial activity and environmental pollution and the operation of hospital services.

Each of these devices is, potentially at least, of considerable importance to politicians and public administrators. Predicting what will happen to the level of unemployment from an increase of income tax can be a much more precise procedure than anybody would have guessed in the days when macroeconomics and differential equations were both considered by the world at large to be secret mysteries. It is sometimes hard to tell from the way in which governments actually behave, and from the air of injured innocence with which they greet predictable consequences of actions taken deliberately but blindly, that the lesson has been absorbed that much of the working of systems even as complicated as social systems is capable of objective analysis, but there has been some progress in this direction.

It may not be surprising that the most useful work has been done in defence, arms control and disarmament, for these are fields in which mathematicians have long been involved with those who are paid for making subjective judgments about imponderable issues. The article by Dr Ian Bellany on page 361 of this issue of *Nature* is yet another illustration of the way in which it is possible to describe mathematically what may be done to throw light on conflicts such as those which exist when opposing nations are asked to make reductions of military forces.

Dr Bellany's conclusions, are unlikely to bring the SALT talks to an immediate end when they are resumed in the new year, but they should help to show how straightforward can be some of the conclusions drawn by mathematicians about military situations. The starting point for Dr Bellany's argument is the assumption that the two sides are to begin with in a state of military balance which can be expressed by the numerical equality of two mathematical functions, each representing the way in which the military strength of each side is determined by parameters such as the size of its standing army, the number of tanks which it possesses and so on.

The argument is chiefly concerned with conventional weapons and with the possibility that there might in the next few years be a serious attempt to bring a balanced reduction of military forces in Central Europe. If the state of balance has been achieved because both sides have reached the point at which they have ceased to invest in new armaments, but are instead content merely to keep their armies up to strength and to replace equipment as it wears out, elementary calculus is enough to show that in any programme for disarmament there should be equal proportional reductions of arms on both sides. The point is important because its validity does not depend on the different ways in which the military strengths of the two sides may be differently determined by armaments of different kinds.

But if each side agrees, for example, to reduce its number of troops and of tanks to go with them by, say, 25 per cent, is there a danger that the outbreak of hostilities would then give one side a better chance of winning by causing damage to its opponent? Simply because defensive positions are frequently safer than offensive postures, it turns out that further conditions must be satisfied by the proportionate reduction of force. Problems like these, in the past few years, have been tackled successfully by means of geometrical multivariate models. This, for example, is the way in which it was shown in the 1950s that a balance of mutual deterrence with ballistic missiles is possible if and only if both sides have more than a certain minimum force—if one side has too few missiles, it can always legitimately fear that these will be destroyed by a pre-emptive strike by the other side, which would then be free to go on and hold the defeated country to ransom. The same argument has more recently been used to demonstrate that multiple independent re-entry vehicles would upset the strategic balance between the United States and the Soviet Union which has been expensively established during the past decade.

By now, there is a distinguished if small body of literature on these and related problems. The late Professor Lewis F. Richardson was one of the most stimulating of contributors, with books such as *Statistics of Deadly Quarrels* (Chicago, 1960). Richardson's chief contribution was to show that differential equations can in many circumstances accurately describe the ways in which an arms race between two close opponents may on some occasions be stable and on some occasions be unstable—in retrospect, for example, it is clear that the principal opponents in the First World War can be accurately described by Richardson's equations. But there are other problems to be considered, notably the economic constraints which increasingly determine the scale on which military forces can be developed in modern states and W. R. Caspary has made distinguished contributions to those aspects of these problems.

In the 1960s, the games theoreticians entered the scene and, in spite of the way in which the name of their craft seems continually to bring them into disrepute among ordinary people (not to mention politicians), nobody will deny that their influence has been stimulating and beneficial. The much maligned Mr Herman Kahn, once described as the "Herman Kahn of strategy", has helped enormously to demonstrate the intellectual interest and importance of mathematical models in military and political conflicts. Politicians who think otherwise should reflect on the value of abstract discussions of how to behave in the game of chicken—that teenage sport in which young people drive headlong towards each other to see which driver loses his nerve first—an unpleasantness for the loser—or whether neither loses his nerve—a greater unpleasantness for both.

PROTEINS

Sighting the Sites

from our Molecular Biology Correspondent

A STRONG contender for this year's *concours d'élégance* of protein chemistry is to be found coyly nestling in the yellow pages of the current issue of the *Biochemical Journal.* This is an article by Green, Konieczny, Toms and Valentine (**125**, 781; 1971), and though it is overtly about the binding of biotin to avidin, both the principles and the results are of much wider relevance.

The background is as follows: avidin is a protein made up of four identical chains, of some 15,000 molecular weight. Each of these has one binding site for biotin, with which it combines with enormous avidity. The only part of the biotin molecule indispensable for binding is the ureido ring. By analogy with what is known about the binding of ligands to enzymes, it might be supposed that the binding site would be situated in a cleft or pit in the surface of the protein. It should be possible, Green and his colleagues reasoned, to find out something about the nature of this cleft, and also about the disposition of the subunits in the tetramer by looking at the interaction of avidin with bifunctional ligands.

Green *et al.* therefore synthesized a series of *bis*biotin derivatives, in which the rings were joined by hydrocarbon chains of different lengths, such that the number of bonds between the biotin carboxyl groups varied between nine and twenty-five. Below some critical chain length it would be supposed that the separation of the biotins would be too short to reach between binding sites on two protein molecules if these extend well below the surface, and indeed it was found that when the number of bonds was anything less than twelve, the bifunctional reagent was able to react with only a monofunctional stoichiometry, and no associated forms of the protein could be detected. At twelve, bifunctional behaviour set in, as judged by the combining ratios and also by the appearance of polymers in the electron microscope. These polymers took the form of linear chains of width corresponding to that of single avidin molecules. The shape of the ligand titration curves (determined by displacement of a dye from the binding site), as well as the ease with which the aggregates could be depolymerized by addition of an excess of ligand, indicated, however, that these chain lengths were barely sufficient for stable cross-linking. The polymers showed few branch points, and being linear, evidently consisted of protein molecules joined by way of two bifunctional ligands to either neighbour. A periodicity corresponding to the width of the avidin tetramer was clearly visible. When the chain length was increased above fourteen bonds, the polymers became more stable, and clear daylight could be discerned between successive units. At very high ligand chain lengths, the polymers became much shorter, betokening the formation of intramolecular links by the *bis*biotin compound.

From these results much of interest can be deduced. The minimum length between the biotin carboxyls that will enable both ends to seat in the active site cavity is 15 Å. Above 17.5 Å the binding strength at both ends becomes comparable with that of the monofunctional ligand. It may thus be deduced that the carboxyl group at the extremity of the ligand locates some 9 Å below the surface of the protein. Moreover it follows from the progressive increase in periodicity of the polymer with ligand chain length, and also of the binding constant within the critical range of chain lengths, that the surface is in some degree compressible. The compression is evidently energetically expensive, and becomes exorbitant below a chain length of twelve bonds. (In long chains, the hydrocarbon, judged by the periodicity, is by no means extended, but obviously increases the thickness of the layers between the protein units.) The length of hydrocarbon at which intramolecular cross-linking sets in also gives a limiting measure of the separation of the binding sites on two subunits within an avidin tetramer. Taking 9 Å as the depth of the carboxyl group, it turns out that the sites must be separated by only 6–10 Å on the surfaces of the subunits. This, of course, could be increased if there were any kind of depression or channel between the sites, to a maximum of about 25 Å.

Contemplation of the possible arrangements of equivalent subunits within a tetramer reveals that they may be related by two-fold or four-fold symmetry (isologous or heterologous association). Only the former can lead to linear polymers, one molecule thick. The four-fold arrangements can lead to two-dimensional networks, or to a unidimensionally repeating system, in which, however, each molecule is associated in zigzag manner to two others. Thus although the subunits are too small to be resolved within the tetramer by electron microscopy, the electron microscope nevertheless discriminates between the possibilities, and establishes the symmetry relation between the subunits, showing them to be arranged in two pairs, tail-to-tail, with a two-fold axis down the middle, and a screw axis relating successive repeating units in the chain. The known accessibility of the bound biotin to biotin-requiring enzymes suggests that it lies in a rather broad cleft, partly exposed, very much like inhibitors in enzymes of known structure.

A fashionable protein, the subunit structure of which confers on it its characteristic biological properties, is concanavalin. The crystal structure is being hotly pursued in two laboratories, and Becker, Reeke and Edelman (*J. Biol. Chem.*, **246**, 6123; 1971) have now deduced from an electron density map of a complex of concanavalin with heavy atom containing ligands the disposition of the saccharide binding sites—arguably the most interesting feature that is to be had from the structure. There are four subunits, each of which possesses one saccharide binding site. The 2.8 Å electron density map shows that

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Lead Ions in the Atmosphere

THE topical subject of cluster ions is aired in next Monday's *Nature Physical Science*, where Castleman and Tang of the Atmospheric Chemistry Research Group at Brookhaven National Laboratory describe the clustering of water molecules on ions of lead. The possible role of ion clusters in the upper atmosphere is receiving increasing attention, so that the laboratory demonstration by Castleman and Tang of the existence of clusters involving lead may soon find an application in theoretical studies on the transport of lead, both radioactive and stable, in the atmosphere. Their data may also account for the low mobility of radioactive lead ions in humid atmospheres.

Briefly, Castleman and Tang passed an ion beam consisting of Pb^+ through a reaction cell in which the concentration of water vapour could be altered, and the products were examined by mass spectrometry. Ions of the form $Pb^+(H_2O)_n$, where n can be as high as seven, were detected. Castleman and Tang find three peaks in the mass spectrometric output for each cluster, corresponding to the major lead isotopes of mass 206, 207 and 208, and the peak corresponding to mass 204 can also be detected.

As well as demonstrating that clustering on lead ions can occur, the experiment has given some of the parameters of the reactions involved. From these data Castleman and Tang are already able to draw some conclusions relevant to the behaviour of lead in the atmosphere. For example, they say that lead ions in the troposphere resulting from the decay of radon will initially exist as clusters, and the species $Pb^+(H_2O)_5$ should be the most abundant. Such cluster ions will be removed by interaction with aerosols or by recombination with negative ions in the atmosphere.

the sites lie in cavities near the subunit interfaces. The tetramer is made up of two roughly ellipsoidal dimers at right angles, and the sites on different dimers are separated by 25 and 35 Å. Depending on the orientation of the sugar groups, which cannot be discerned at this resolution, two bound saccharides on one tetramer could be up to 47 Å apart—a rather small but feasible distance for the approach of agglutinating cell surfaces.

HUMAN EVOLUTION

Darwin Centenary

On October 28–30, Rome was the setting for another celebration of the centenary of the publication of the *Descent of Man* by Charles Darwin (see last week's issue: **234**, 251; 1971). The occasion was marked by a distinguished gathering of international scientists at the Palazza Farnesina, home of the Accademia Nazionale dei Lincei. The Lincei is one of the oldest European scientific societies whose membership encompasses the broad sweep of natural philosophy in its true sense; no more suitable venue could be envisaged for a meeting that ranged so widely.

After a welcome by the President of the Lincei, Professor Beniamino Segre, and an introduction by Professor C. Barigozzi, the first session was addressed by Professor T. Dobzhansky (Rockefeller University) and Professor E. Mayr (Harvard University). Professor Dobzhansky, in a wide and deep analysis, emphasized the relative lack of differences between man and apes that are being shown by recent work in comparative biochemistry, but he also drew attention to the overriding distinctiveness of human culture in terms of symbolism, language, self awareness and death awareness. Plasticity of nongenetically determined behaviour was seen as a better adaptive strategy than fixity of behaviour in genes. Man, he insisted, is not a chance animal and natural selection is not a chance process but a feedback servo-mechanism between the gene pool and the environment. If variability is present between forms, natural selection must occur and innovative genotypes will be directional and lead to a closer fit with the environment. Evolution was seen as a synthesis of determinism and chance, a synthesis that is in itself creative.

Professor Mayr drew attention to the fact that much of the *Descent of Man* was concerned with sexual selection, and that this was rejected as an evolutionary process by many of Darwin's critics; he supported sexual selection by showing that it can confer reproductive advantage and lead to sexual dimorphism. On the other hand Professor Mayr could not agree that sexual selection has played an important part in the development of human races but accepted that it may account for the acceleration of the process.

The afternoon of the first day was the turn of the "fossil men". Professor P. V. Tobias (University of Witwatersrand) gave a historical résumé of the evolution of the genus *Homo* in which he supported Darwin's prediction of Africa as the cradle of mankind, and took the opportunity of announcing the find of a new australopithecine skull in the breccia at Sterkfontein. In almost direct contradiction Professor G. H. R. von Koenigswald (Senckenberg Museum, Frankfurt) reviewed the oldest hominid fossils from the Far East and, after denying the hominid status of *Kenyapithecus wickerii*, postulated an Indian centre of dispersal of the early hominids in two directions towards Africa and Java. This viewpoint was succinctly countered by Professor Tobias, in discussion, by the remark that palaeontologists must work with the fossils that they have and not those that are not yet to be found!

In the same session Dr M. H. Day (Middlesex Hospital Medical School, London) reviewed the early evolution of *Homo sapiens* in the light of the recent finds from the Omo Valley in Ethiopia. He emphasized the spectrum of forms that are emerging from the fossil record and contended that the mosaic process is becoming more and more apparent in this phase of human evolution. On the one hand, the *erectus*-like sapients such as Vértesszöllös, Omo II, Solo and Rhodesian form a "pithecanthropoid intermediate" group and on the other hand there is a group which includes Swanscombe, Steinheim, Skhul and Amud that could remain as "neanderthaloid intermediates".

The second day was the turn of the geneticists and behavioural scientists and included Dr G. A. Harrison (University of Oxford), Dr K. K. Kidd (University of California), Dr J. H. Crook (University of Bristol) and Professor L. Balout (Paris). Dr Harrison emphasized the influence of population genetics on evolutionary thinking and Professor Balout outlined the unity and continuity of stone tool cultures by breaking down a number of the artificial barriers that have been placed between cultural stages.

The final day included sessions on art and communication as well as the relationship between evolution and

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More Ribosome Binding Sites Sequenced

The three sites at which ribosomes bind when they initiate the translation of the three cistrons of bacteriophage R17 RNA and the binding site for the phage $Q\beta$ coat protein cistron were sequenced in 1969 by Steitz and by Hindley and Staples. In next week's *Nature New Biology*, Staples and Hindley and Staples, Hindley, Billeter and Weissmann report the base sequences of the two other $Q\beta$ ribosome binding sites, those of the $Q\beta$ replicase and the $Q\beta$ assembly protein. But although the sequence of six initiation sites in two messenger RNAs is now known, it is not possible to formulate a clear picture of how a ribosome recognizes an AUG codon at the beginning of a genetic message and correctly initiates translation.

There are two obvious ways in which, in theory at least, a ribosome might be able to differentiate between an AUG codon acting as an initiator and specifying formyl-methionine and an AUG codon internal in a genetic message which specifies methionine. One is that the initiator AUG codon might be in a region of the messenger with a specific and recognizable secondary structure; the other is that the initiator AUG codon might be preceded by some particular sequence of bases which the ribosome can recognize. The six initiation sites so far analysed do not, however, indicate any common secondary structure, neither do they reveal a common base sequence which might signal initiation. All that can be said for the moment is that the sequence immediately preceding an initiator AUG is rich in purines. In short, there must be some molecular basis for the specificity of chain initiation, but, as Staples and Hindley say, "Knowledge of the six initiation sequences of $Q\beta$ and R17 does not define the reason for this specificity".

Also in next week's *Nature New Biology*, Kozak and Nathans make the intriguing suggestion that the so-called assembly (on maturation) proteins of the RNA phages may act as regulators of translation of the phage cistrons. They report a series of experiments which indicate that on infection the bacteriophage RNA enters an *Escherichia coli* still associated with assembly protein. They postulate that either the assembly protein plays some part in "threading" the phage RNA through an F-pilus or, once in the cell, it may block the translation of all but the replicase cistron, such that at early times replicase rather than coat or assembly proteins are made. There is, of course, a precedent for this suggestion; late in infection phage coat protein blocks the translation of the replicase cistron. This effect of coat protein can be detected *in vitro* and no doubt Kozak and Nathans are currently trying to test with cell free systems their notion that assembly protein blocks the translation of the coat protein cistron.

theology. Interest in evolution remains high in both popular and scientific circles, and the Lincei was shrewd to catch the mood of the times by attracting a broadly based group of speakers each of whom had something important to contribute towards a better understanding of man's evolutionary history.

CLIMATE

Advance of Sahara

MUCH of the blame for the advance of the northern Sahara has traditionally been laid at the door of man, whose crude farming techniques have, since Roman times at least, created erosion and desert conditions in once fertile regions. A report by the World Meteorological Organization has now placed this belief on a scientific footing and it provides quantitative data on the importance of man's activities to the fertility of the region (H. Flohn and M. Ketata, *WMO Technical Note* 116, WMO, Geneva, 1971).

In addition to the detrimental effect of man, natural climatic changes also produce fluctuations in desert margins. In the Sahara it seems that the overall trend during the past 7,000 years is for the desert to dry up and expand (see, for example, J. L. Cloudsley-Thompson, *Internat. J. Envir. Studies*, **2**, 35; 1971), but this is not to say that farming activity is not important in the short term. During periods of delicate balance between the needs of vegetation and rainfall, overgrazing and the utilization of firewood can have a disastrous and irreversible effect.

The use of artesian wells and the intensive farming of date palms have a dramatic effect on the water balance. Since 1881 the number of date palms in the border region of the Tunisian Sahara has increased by more than 50 per cent. Flohn and Ketata estimate that the effect of this increase has been to reduce the level of subterranean water at a rate of 5 cm per year. Over a period of less than 100 years, it seems likely that effects of this magnitude will dominate over the long term natural climatic variations. As well as the direct effect on evapotranspiration of the economic importance of the palm, other farming techniques encourage the growth of the desert; notably, overgrazing and compacting of the soil by domestic animals such as the goat cause erosion. Even now, however, it may not be too late to take steps to rectify the situation, at least partially. At one farm site north of Nefta, an area of 50 hectares has been protected by barbed wire for the past 60 years. Here, the original vegetation has apparently been restored, with an average soil coverage of more than 80 per cent, a figure which contrasts dramatically with 5 per cent coverage by the degraded vegetation on the other side of the fence.

The report concludes that the historically observed progress of desertic conditions towards the north is caused "not by a natural fluctuation in climatic conditions, but by human interference". Clearly, all activities involving the delicate water balance in the intermediate zone between desert and cultivated land should be carefully planned and coordinated to avoid further adverse effects on the water budget. In particular, caution over the extended use of artesian water and irrigation, encouragement of dry farming (such as olive farming), reafforestation and increase of animal husbandry to allow the return of natural vegetation could do much to redress the balance.

HAEMATOLOGY

Sickle Cell and Flight

from a Correspondent

IT has been known for about twenty years that aircraft flights can cause illness among people with sickle cell disorders—a hereditary disorder of the blood that affects negro populations. But many negroes have only mild forms of the disease and are unaware that they are sufferers. To what extent are these people at risk when they embark on an aircraft flight?

Recent work on this question has been published in the *British Medical Journal* (**4**, 593; 1971) by R. L. Green, R. G. Huntsman and G. R. Serjeant, who suggest that all negroes should be screened for sickle cell disorder before flying. The problem arises because even modern jet aircraft are not fully pressurized as compared with ground level—the cabin pressure in a Boeing 707 at cruising altitude corresponds to an altitude of 5,000 to 7,000 feet—and many scheduled African flights still use unpressurized aircraft.

Sickle cell disease is an abnormality of the haemoglobin molecule. Several forms have been described; for example, substitution on the peptide chain of valine for glutamic acid results in production of haemoglobin S instead of the normal form, haemoglobin A, and another form which Green *et al.* found to be relevant to their studies is haemoglobin C. The abnormal haemoglobin renders the shape of the red blood corpuscles less stable and under conditions of low oxygen tension the

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Reading through a UGA Terminator

THE closely related group of RNA phages which include R17, MS2 and f2 possess genomes which specify only three proteins, namely coat and assembly proteins, which form part of the viral capsid, and a subunit of the viral replicase. The phage $Q\beta$, which is not in the same serological subgroup as R17 and its relatives, specifies coat and assembly proteins and a replicase subunit but, in addition, a fourth protein known as A_1 or II*b*, which weighs 36–38,000 daltons, can be recovered from $Q\beta$ phage particles.

What is the nature of this fourth protein? According to the experiments of Weiner and Weber and of Moore *et al.* reported in next Wednesday's *Nature New Biology*, it is a larger than life coat protein made when ribosomes fail to terminate synthesis at the end of the coat protein cistron and continue to translate the intercistronic divide and part of the next cistron, which specifies a subunit of the replicase.

Moore *et al.* have shown that the first five amino-acids of A_1 are the same as coat protein and Weiner and Weber have shown that the first eight amino-acids of A_1 (or II*b*) are the same as the coat protein. Furthermore, Weiner and Weber report that A_1 contains tryptophan, histidine and methionine, amino-acids not in the $Q\beta$ coat protein, and that A_1 is never synthesized by mutant $Q\beta$ phage with an amber mutation in their coat protein cistron.

These data indicate that A_1 is probably produced when ribosomes read through the termination signal at the end of the $Q\beta$ coat protein cistron. Because amber (UAG) and ochre (UAA) codons are efficient terminators unlikely to allow read-through, both groups argue that the terminator codon at the end of the $Q\beta$ coat cistron is probably a solitary UGA codon, for UGA codons are known to be leaky terminators. Horiuchi *et al.* (*Virology*, **45**, 429; 1971) have also recently reached this conclusion and Weiner and Weber report experiments with a UGA suppressor strain of *Escherichia coli* which confirm it. They find that the molar fraction of A_1 (II*b*) protein in $Q\beta$ phage particles increases from 2 per cent to 7 per cent when the phage are grown on a UGA suppressor strain of *E. coli*. Furthermore, introduction of a streptomycin resistance mutation, which reduces the leakiness of UGA termination, reduces by about 30 per cent the yield of A_1.

The A_1 protein is about 2.5 times the size of coat protein, which means it has about 200 amino-acids in excess, and yet it can apparently become incorporated into the phage particles. It will be interesting to learn how this is achieved and how much of the replicase subunit sequence is found in the A_1 chain.

corpuscles—normally biconcave disks—are distorted into sickle-shaped cells. These cells clump together and block the lumen of the smallest blood vessels, impeding the flow of blood. The reduced oxygen supply leads to necrosis of the tissue, which most commonly occurs in the small vessels of the spleen where it causes severe abdominal pain.

Green *et al.* describe seven patients who suffered sickling crises during flight—one of whom was only a carrier of the disease but flew in an unpressurized aircraft at high altitude. The others were all homozygous for the disorder, but three of them aged between 22 and 48 had suffered no previous symptoms and were unaware that they had the disease. One interesting case involved a 15-year-old Jamaican girl known to have sickle cell disease of the haemoglobin C variety who first encountered the symptoms during a flight to Mexico City. Her symptoms persisted for five days until she moved to sea level at Acapulco.

Oddly enough, negroes with severe sickle cell anaemia may have fewer problems in flying than those with mild forms. This possibility arises because sufferers from the severe form of the disease have had so many similar episodes arising from minor provocations—such as respiratory infections—during childhood that much of the spleen has already been infarcted. This means that the flow through the small vessels of the spleen has already been largely cut out. A further factor in such patients is that they are anaemic from the constant destruction of red blood corpuscles by sickling so that their blood flow is less viscous and less likely to become blocked. The most severe effects during flight are seen in those sufferers with haemoglobin C who are normally asymptomatic and not anaemic, and whose blood is of comparatively high viscosity.

Should there therefore be a revision of the 1961 recommendations of the Aerospace Medical Association which say that travellers with severe sickle cell anaemia or with haemoglobin C should not fly? In one sense these recommendations seem draconian in that sufferers from severe sickle cell disease may face little risk, and the recommendations may be an unnecessary obstacle to these negro travellers. In view of the findings of Green *et al.*, however, the recommendation with respect to haemoglobin C seems fully justified.

The problem is that of ensuring that travellers do not have the asymptomatic form of the disease. Hospitals already carry out screening procedures on patients of negro origin who are to be given anaesthetics, for severe sickling can occur if the oxygen tension is allowed to fall under anaesthesia. When the possibility of sickling is anticipated, it can be prevented by giving high oxygen concentrations and intravenous sodium bicarbonate. The screening technique involves the microscopic examination of blood films under reduced oxygen pressure. If the characteristic sickling is seen, the exact type of disorder can be determined by electrophoresis. It may be that all prospective negro travellers should be screened in this way—certainly screening is essential for all aircrews.

CELL TRANSFORMATION

Surfaces Involved

from our Cell Biology Correspondent

TUMOUR virologists are, of course, always on the lookout for new parameters which they can measure and thereby decide whether a cell is transformed or untransformed. The classical parameter, the continued division of transformed cells in environments which severely restrict or totally inhibit the

Distinguishing Atlantic Cherts

ONE of the many unexpected results to emerge from the JOIDES Deep Sea Drilling Project has been the discovery of cherts in drill cores over a wide area of the north Atlantic. But what exactly are cherts? In general terms they are highly siliceous rocks comprising microcrystalline quartz and/or chalcedony—the chalcedony serving to distinguish them from other forms of sedimentary silica. On the other hand, Rex (in *Initial Reports Deep Sea Drilling Project*, Vols. 1 and 2; 1969 and 1970), in his preliminary report of Legs 1 and 2 of the JOIDES Project, included within the term chert rocks composed of cristobalite, a rather different form of SiO_2. Thus although there is no doubt about the general definition of chert, the overall term covers differences in petrological detail.

Definitions as such are perhaps not too important except in so far as differences in petrological detail may conceal significant differences in origin. The upper Jurassic to middle Miocene cherts discovered in the Atlantic during Legs 1 and 2 of the JOIDES Project, for example, are widespread and occur in a wide variety of sediments including radiolarian oozes, nannoplanktonic chalks, zeolitic clays and foraminiferal silts. For these reasons alone, therefore, they are clearly important; and petrological differences are likely to imply differences in formation which could be significant. The recognition of such differences is thus critical, not least because the cherts have sometimes been correlated with seismic horizon A.

In next Monday's *Nature Physical Science* Calvert reports further on this theme. He confirms that the two forms of chert are clearly in evidence in the Atlantic but prefers to limit the term chert to the quartz-containing variety. The true cherts are thus the pre-upper Cretaceous samples whereas the younger "cherts" are, on the evidence of X-ray diffraction and infrared absorption data presented by Calvert, composed largely of disordered α-cristobalite.

It further emerges that the infrared absorption and X-ray diffraction spectra from the north Atlantic "cherts" are identical with those reported from siliceous concretions in Tertiary volcanic sequences, porcelanites from the Miocene Monterey Formation and certain common opals. In short, such silica structures are quite common in younger geological formations, are distinguishable from true cherts and, in Calvert's view, are better referred to as porcelanites. The origin of these porcelanites is not yet clear, however.

The classic definition of chert includes the possibilities of both organic and precipitate origin—and this may be relevant here too. For example, Ernst and Calvert (*Amer. J. Sci.*, **267A**, 114; 1969) regard the Monterey porcelanites as "an intermediate phase in the diagenetic modification of biogenous silica (diatomite) to chert, a phase which is not preserved in older (pre-Cenozoic) formations". The north Atlantic porcelanites may be similar; but they could equally well be alteration products of volcanic debris.

AQUATIC BIOLOGY

New Unit

A NEW Unit of Aquatic Pathobiology has been established at the University of Stirling with the help of a grant of £76,000 from the Nuffield Foundation. The director will be Dr R. J. Roberts, who is at present at the University of Glasgow. The university has on its campus a twenty-four-acre loch, an aquarium, and is close to the Forth estuary, so that the unit will be ideally situated for research on fish pathology, a field in which there is at present a need for far more research, particularly in connexion with the growing industry of fish culture. There is also a shortage of veterinary and scientific staff qualified in the field, and in this regard the new unit will have a programme of teaching at both the undergraduate and postgraduate level.

multiplication of untransformed cells, has proved and still proves to be enormously useful but tumour virologists are increasingly exploiting additional biochemical parameters.

Rubin and his colleagues, for example, have recently established that chick cells transformed by Rous sarcoma virus take up glucose and 2-deoxyglucose from their medium at a faster rate than untransformed cells although the rate of uptake of these sugars also depends on a cell's physiological state and in particular the rate at which it is dividing. This second observation raised doubts as to the relationship between enhanced uptake of sugars and transformation *per se*, but now Martin, Venuta, Weber and Rubin (*Proc. US Nat. Acad. Sci.*, **68**, 2739; 1971) have, by exploiting the temperature sensitive mutant T5 of Rous sarcoma virus isolated by Martin (*Nature*, **227**, 1021; 1970), shown that the increased rate of uptake of 2-deoxyglucose by transformed cells indeed depends on the expression of the transforming Rous sarcoma genome.

They report that when chick cells transformed by Rous virus and untransformed cells are growing at the same rate the transformed cells take up 2-deoxyglucose at a rate which is three times faster than the untransformed cells. Cells transformed by the mutant T5 and cultured at the permissive temperature of 36° C behave like cells transformed by wild type virus. But when mutant transformants are shifted to the nonpermissive temperature, 42° C, the rate at which they take up this sugar falls, without any detectable lag, such that by 12–24 hours after the shift the rate is that of untransformed cells. And when the transformants are returned to 36° C their rate of uptake once more increases. In short, transformed cells growing in the same conditions as untransformed cells exhibit a faster rate of uptake of 2-deoxyglucose and this difference depends, however indirectly, on the continued expression of the transforming Rous sarcoma genome. Furthermore, as experiments with cytosine arabinoside prove, the enhanced uptake of sugars by transformed cells is not dependent on DNA synthesis.

The mechanism which regulates the rate at which sugars are taken up by cells may well involve changes in the chemistry of the cell surface, a most fashionable subject for investigation among tumour virologists these days. Sachs and his colleagues, for example, report in the same issue of the *Proceedings* (*ibid.*, 2748) their latest experiments with concanavalin A and other lectins. They claim that SV40 transformed cells cultured at 24° C are much more readily agglutinated by concanavalin A than untransformed cells but at 4° C this difference between transformed and untransformed cells cannot be detected; neither are agglutinated. At both 24° C and 4° C, however, both transformed and untransformed cells bind the same amounts of concanavalin A. Furthermore, after exposure to trypsin at 24° C untransformed cells are agglutinated by low concentrations of concanavalin A but after exposure to trypsin at 4° C neither transformed nor untransformed cells are agglutinated by low concentrations of this lectin.

From these data Inbar, Ben Bassat and Sachs argue that the sites which bind concanavalin A are not affected by temperature changes but the component of these sites which determines agglutination is temperature sensitive and transformation sensitive. The agglutination sites may well be associated therefore with some specific metabolic activity. Inbar *et al.* comment that this conclusion does not hold for two other lectin binding sites, those for wheat germ agglutinin and soybean agglutinin, which are not apparently temperature sensitive. And what is perhaps even more intriguing, Sachs and his colleagues remark that there is a correlation between the activity of the component of the concanavalin sites that is involved in agglutination and the malignancy of a cell; but that is to be another story.

T Cell Activation by Histocompatibility Antigens

THE general concept that lymphocytes of the mouse can profitably be classified as either T or B cells is now widely accepted. T cells are easily defined as those lymphocytes which have undergone differentiation in the thymus; their precursors moved to the thymus from either the bone marrow in an adult or an equivalent haematopoietic organ, probably the liver, in the foetus. The definition of B cells is less easy because it is by no means certain whether the mature B cell arises in the bone marrow or from a precursor cell which must leave the marrow to undergo proliferation and specific differentiation elsewhere. Functionally, however, the B cell seems, unlike the T cell, to have the capacity to differentiate into an antibody secreting cell and thus in spite of its slightly murky origins it can usefully be delineated as a cell species.

The functional characteristics of T cells are still a matter of some dispute and the arguments concerning them touch on the fundamental question of whether the immune process is instructive or selective. Most immunologists favour some form of selective mechanism, whereby an immune response proceeds because of selection from a heterogeneous cell population of those cells best equipped to deal with a particular antigen. The nature of the heterogeneity in this last instance is one of the central problems of immunology. Sprent and Miller, in an article in next Wednesday's *Nature New Biology*, study these problems and reveal how the careless adoption of a word can lead to unorthodoxy.

The Australian school of lymphocyte function has contributed much to the literature in recent years. Among their efforts has been the demonstration that when thymocytes along with an antigen, often heterologous erythrocytes, are injected into mice which have been lethally irradiated, the injected cells react to the antigen by blast cell transformation; when transferred, along with more antigen, from the primary host spleen into a secondary irradiated animal the reacting cells display a specific capacity to cooperate in the ensuing immune response. The procedure at one time was referred to as "education". The full semantic horror of this nomenclature has now been realized, and Sprent and Miller offer "activation" as the preferred alternative.

Sprent and Miller describe the injection of parental strain thymocytes or thoracic duct lymphocytes into lethally irradiated F_1 hybrid mice. The injected cells proliferate in response to the antigens, foreign to them, of the other component of the hybrid and, after a period of intensive activity in the spleen and mesenteric lymph nodes, blast cells appear in the thoracic duct lymph.

These primed cells, when transferred to a second similar hybrid recipient, are capable of responding more quickly than a comparable unprimed thoracic duct lymphocyte population and, more interestingly, are much less capable of responding to a third party antigen—in an appropriate hybrid recipient—than are unprimed cells. The process of activation thus either involves selection of a specifically reactive cell population or it involves rapid restriction of an initially wider reaction potential.

It is interesting that activated parental cells collected from the thoracic duct of F_1 irradiated mice did not induce a splenomegaly reaction when injected into appropriate newborn F_1 recipients, and it was impossible to demonstrate the activated state beyond second transfer into irradiated F_1 recipients. This finding, which suggests a restriction on the proliferative capacity of T cells in response to continued antigenic stimulus, contrasts with the suggestion (Askonas *et al.*, *Proc. US Nat. Acad. Sci.*, **67**, 1398; 1970) that B cell populations have a capacity for repeated response to antigenic stimulus during a series of transfers in irradiated host mice.

Dental Plaque and Oral Health

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Oral diseases in man, such as periodontitis and dental caries, are not caused by single pathogenic organisms but appear to be the result of the complex biological interactions of the various organisms of which dental plaque is composed.

DISEASES of the teeth and their supporting structures are more widespread than any other disease. Chronic periodontitis, the principal cause of tooth loss, is a chronic inflammatory process involving gradual destruction of the supporting tissues of the teeth, and almost as prevalent is dental caries, the familiar tooth decay. In spite of continuing, intensive research, we are, in some respects, as far away as ever from a clear understanding of the aetiology, pathology and prevention of these two diseases. Perhaps the most intriguing aspect concerns a factor common to both diseases: the dental plaque.

It is now more than seventy years since the terms "gelatinous microbial plaques" and "feltlike mass" were introduced[1,2] to describe the closely-packed mass of microorganisms present on the natural erupted tooth surface. Since that time, extensive effort has failed to implicate any single one of its constituent species as being the sole cause of either disease in man.

Host-Flora Relationships

It is possible that in our assessment of plaque we have failed to consider it as forming just one part of the body flora. This flora does not normally produce disease but, on the contrary, maintains a commensal or symbiotic relationship with the human host and is involved in several functions, including the digestive processes and the prevention of the establishment in the body of alien pathogens. If we extend this concept to other fields of microbiology, we soon discover that not only is plaque unexceptional, but that most surfaces have their own individual flora, a balanced microbiota living in dynamic equilibrium with its host. Many conclusions in bacteriological studies are based upon the activities of organisms grown in pure culture and it is worth emphasizing that organisms in their natural environment are often closely related to one another physically and tend to exhibit interdependence to a greater or lesser degree. Conclusions drawn from such measurements as the rate of reproduction of organisms in pure culture probably bear no relation to the state of affairs pertaining in a "natural" habitat. Recently it has became apparent[3] that the rate of turnover of organisms in plaque may be less than that of organisms grown in pure culture under optimal metabolic conditions.

Microbial Communities

Plaque may represent a primitive example of community development, that is, of individual unrelated organisms living together for their mutual benefit. Certainly the organisms in plaque are packed as closely together as those in a centrifuged colony of a pure culture[4,5]. It would seem reasonable to suggest that the evolutionary process has led to a situation in which many different species of microorganisms have developed the capacity to live commensally or symbiotically with one another in communities such as the plaque, despite very close spatial relationships. Recent freeze-etch studies in our own laboratory would seem to indicate that this close packing is not artefactual, because the rapid freezing involved averts shrinkage due to dehydration.

Plaque Structure

Relatively little information about the structural organization of plaque is at present available. Its outstanding structural feature—that is, filaments orientated parallel to each other and at right angles to the tooth surface—was first noted by Williams[2]. Observations in our laboratory on paraffin sections, and using scanning, freeze-etch and transmission electron microscopy, indicate that smaller organisms are constrained to grow between filaments and may become attached to them, giving rise to the appearance sometimes described as *Leptothrix racemosa*. Ultrasonication for periods of up to 0.5 h has demonstrated the firmness of attachment of coccal and other forms to filaments[6]. This relationship is probably responsible for the appearance of "rosettes" on electron micrographs of the outer (salivary) surface of plaque, where a group of coccal forms is arranged around a central filamentous organism[6–8].

Structure and Function

Provided that one accepts the initial random distribution of organisms in plaque, the close packing to which we have alluded would seem to imply the existence of one or both of two phenomena in the crucial stagnation sites implicated in caries and chronic periodontitis. Either the same organisms undergo a change in their metabolic pathways or different organisms become active because of a change in environment. Anaerobes, rather than aerobes, tend to be favoured by the increasing stagnation and decreasing oxygen tension and most plaque organisms are, in fact, facultative anaerobes[9,10], possessing both acidogenic and proteolytic potential. This consideration becomes of greater significance in the light of work in progress in Bristol and elsewhere, which would seem to suggest that the structure of plaque changes as it approaches the contact area or gingival margin but tends to show relatively constant structural features for a given thickness and for a given distance from the stagnation site. As the area in question becomes gradually less accessible to cleansing forces, it would appear that the undisturbed plaque increases in thickness and that, during this process, organisms at the enamel surface align themselves parallel to each other and at right angles to the tooth surface, and grow directly towards the plaque–saliva interface (presumably because this method of growth is suited to their nutrition[6,7]). The fact that the site below the contact area between teeth is the most stagnant on enamel smooth surfaces must contribute to the known onset of both caries and inflammatory periodontal disease in this region. With regard to stagnation sites, it is of interest that, in peoples living on crude diets, adjoining approximal surfaces frequently show marked wear facets indicative of heavy masticatory forces. This wear reduces the interstitial stagnation sites and also the areas of approximal tooth surface available to plaque. At the same time the heavy masticatory activity eliminates pits and fissures on occlusal surfaces, further reducing potential stagnation sites. Thus the low caries incidence in such peoples is related to both eating habits and low, refined carbohydrate intake. The significance of this would seem to be that the advent of a diet containing foods lacking in fibrous texture and overburdened with fermentable carbohydrate has been the principal factor contributing to the production of a focal point, interstitially, for the initiation of the two disease processes under discussion. Fissure plaque would seem to differ essentially from smooth surface plaque only in the limitations imposed on its size by its anatomical site[11,12].

Acid and Caries

The principal problem in plaque research has always been to explain its involvement in the production of caries and chronic inflammatory periodontal disease. Since the early work of Miller[13] the concept of acid demineralization as the essential feature in the production of the carious lesion remains unchanged. It has been demonstrated[14] that plaque lactobacilli and some streptococci form more acid in media containing enamel or dentine than in control cultures not containing tooth substance. More than one acid is, however, produced in plaque, and by many different organisms[10,15–18]. Lactic acid has frequently been cited as the principal causative agent in caries, but it has been shown recently[15,17,18] that other organic acids may also make important contributions.

Recent work[19] on the destructive mechanism in dental caries has shown that the dividing line between acid demineralization and chelation may be much finer than was previously thought to be the case. In addition, attention has been drawn to oxidation-reduction potentials[20], electrolysis (P. Critchley, personal communication, 1970) and electrical potentials[21,22], as well as straightforward diffusion phenomena, as factors relevant to the pathogenesis of caries. It has been suggested[23] that, in a normal healthy mouth, slight mineral loss due to acids generated in the plaque is followed by mineral deposition. Under cariogenic conditions, dissolution is greater than deposition and one way of helping to boost the restorative role of the plaque might be the precipitation of insoluble calcium salts on the enamel surface, especially in stagnation areas. It has been suggested[24,25] that the incidence of caries-like lesions in animals other than man points to an aetiological mechanism other than the production of acid from refined carbohydrate. The incidence of caries in animals is, however, extremely low and caries in other than "civilized" man has been shown to have a different pathogenetic basis[26], often being secondary to fracture of worn enamel and resultant food impaction.

The phenomenon of biogenic acid dissolution of mineral is not confined to the human oral cavity. Other workers[27,28] have stressed the biologically fundamental nature of acid dissolution of minerals from an evolutionary standpoint. It has been noted[25] that certain marine organisms can bore into rock, shell and coral, and that living forms as different as algae, sponges, flatworms and snails are able to dissolve calcium-containing and other minerals chemically. The pre-eminence of phosphate as a limiting factor in cell metabolism has also been emphasized[25,27].

The use of elements such as phosphorus in the production of high energy bonds for metabolic requirements is well known. It has been suggested[29–34] that the typical calcium phosphate skeleton evolved originally as a simple means of localizing phosphate for energy purposes. An increasing body of evidence is becoming available which would seem to indicate that the production of acid within plaque is closely related to the requirements of plaque microorganisms for phosphate. Thus it has been found[35] that plaque inorganic phosphate levels are inversely proportional to caries incidence and that a high flow rate of parotid saliva appeared to be related to higher plaque phosphate levels and a lower incidence of caries. It has been shown[36] that acid production increases with thickness of plaque and[37] that plaque bacteria considerably modify the pattern of acid attack.

Our calculations show that only an infinitesimal amount of acid is required to produce the degree of demineralization that occurs in an average carious lesion—far less than is normally available in impacted food debris or as a result of microbial metabolism in the established plaque. A clearer explanation is hindered by the multiplicity of phenomena involved. At all events, the remineralization, which is a feature of arrested caries, would seem to indicate that demineralization and remineralization are usually in equilibrium. It is conceivable that calcium and phosphorus removed from the tooth by bacterial activity under non-pathological circumstances are replenished from the saliva, and that, although enamel as such possesses no physiological capacity for repair, salivary calcium and phosphorus probably constitute a very efficient repair mechanism[23].

Polysaccharides in Plaque

Considerable attention has recently been focused on yet another biochemical feature of plaque, its intra- and extracellular polysaccharide content, especially the highly branched dextrans. Plaque dextrans are now regarded as having two chief functions: the maintenance of the structural integrity of plaque by their inherent stickiness and high degree of branching, and their use as an energy storage product when the supply of simple sugars and laevans is exhausted. This view of the function of dextrans and associated polysaccharides in plaque metabolism may, however, have been oversimplified. In general, biochemical end-products may be regarded as the result of particular metabolic pathways aimed at the survival of the organisms involved. Thus it has been suggested[3,38] that least dextran is formed under conditions most favourable for bacterial growth. It has also been proposed[38] that dextran might be used by bacteria as a means of concentrating ions or other essential nutrients. (Attempts are now being made to synthesize a particular polysaccharide in commercial quantities, for use in dealing with water pollution; this consists of glucose and some galactose, derived from the pseudomonad *Zooglea ramigera*, and is useful because of its ability to adsorb large amounts of metal ions and organic material[39].) Other workers have noted the relative inertness of plaque dextrans, and the extent to which they limit intercellular diffusion. The presence of polysaccharide matrices around individual organisms in pond slime has been described[40], and it has been suggested that, by means of this "shell", individual microorganisms are able to obtain physical and chemical protection from noxious agents in the environment. The last of these findings may be of considerable importance in plaque metabolism, because concentrations of sucrose—that highly cariogenic agent—inhibit most bacteria when present in excess.

Thus the information at present available suggests that plaque bacteria produce dextran and similar polysaccharides to deal with the problem of large quantities of fermentable carbohydrate and, possibly, also acid end-products, and to bind essential organic and inorganic nutrients which are only present in small quantities. In these circumstances, the viability of inner plaque may depend upon the diffusion of nutrient material along filaments rather than through the interbacterial matrix[6].

Chronic Periodontitis

Organisms which are farthest removed from the saliva–plaque interface are also at the greatest distance from a source of readily available nutrients[25]. Attention has been drawn[41] to the ability of plaque organisms to utilize whatever substrate is available, and it has been suggested[41] that metabolism of a proteinaceous substrate would result in an alkaline environment favouring calcium formation, whereas the presence of fermentable carbohydrate would favour the production of an acid environment and caries. It has been pointed out previously that the two disease processes are initiated in close proximity to one another on the smooth surfaces of teeth. If the diet of the host contains little fermentable carbohydrate, mouth organisms must be dependent for their growth and reproduction on products of saliva, epithelium, gingival fluid and food debris. Thus the most gingivally situated plaque is in relation to an epithelium with a high rate of turnover and it might be expected to produce the agents which will also be most likely to initiate chronic periodontitis[42,43] because of their digestion of epithelial protein.

In the light of recent findings[3,38] it seems most likely that, in the deeper layers of plaque, there is frequently insufficient nitrogen available for cell growth and division, and that the consequence of this metabolic blockage is a build-up at each stage of the process; there is, therefore, an accumulation of acids and polysaccharide where fermentable carbohydrate is present. The only readily identifiable product is the polysaccharide and this may explain why attention has so far been directed at the polysaccharide rather than at an understanding of the underlying metabolic implications of its presence. When fermentable carbohydrate is not present, damage to the teeth as a result of caries becomes very unlikely. The ubiquitous nature of plaque compared with fermentable carbohydrate might possibly explain why chronic periodontitis is more widespread than caries.

Conclusions

It would seem to be a reasonable proposition that the natural tendency for organic material, both biotic and abiotic, to be adsorbed on inorganic surfaces has favoured cell growth. This appears to be reflected in the situation existing in the mouth, where bacteria and salivary pellicle are being deposited continuously on available erupted enamel surfaces. In this way organic nutrients may be localized to the advantage of the organisms concerned.

Similarly, bacterial phosphate requirements seem to be favoured by their adsorption on tooth surfaces. There may be a link with a possible mechanism of enamel "protection", whereby mineral lost as a result of microbial activity is replaced by salivary calcium and phosphate. In the evolutionary scale, the tendency has been for higher organisms to acquire salivary glands and to lose numbers of dentitions; this may be significant, not only as far as mastication, which is a function of mammals, is concerned, but also in relation to maintenance of the integrity of the tooth surface.

The caries process may be regarded as due to the effects of organic acids normally used as energy sources in the production of proteins and other components essential to microbial cell growth and division. But carbohydrates as such represent potential energy, whereas the various acids represent kinetic energy and are involved in several stages of different biochemical cycles.

The onset of chronic inflammatory periodontal disease, on the other hand, may be attributed to the activities of bacteria which will utilize gingival epithelium as a substrate and will therefore damage the periodontium, unless the nature of the diet and the oral hygiene of the patient are such that a build-up of plaque at the gingival margin is prevented.

Controversial though some of these concepts of plaque may seem, it is essential, in our opinion, to realize that we are dealing, not with a straightforward pathological entity, but with a complex ecological phenomenon, many of whose features are common to other microbial communities. This should, in turn, influence our approach to the treatment of caries and chronic periodontitis because it becomes a question, not of haphazardly and maybe dangerously interfering with the balance of the oral microbiota (a factor of considerable importance in the maintenance of health) but of modifying the diet or the plaque without the use of antiseptics, antibiotics or other agents which are likely to produce cures worse than the diseases.

Comprehensive reviews of the subject have recently been published[41,45].

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Chemical Constituents of Interstellar Clouds

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The application of organic chemistry to the interstellar medium has considerably heightened the appreciation of the complexity and variety of interstellar clouds. Results obtained during the past three years suggest that only a start has been made in the identification of the molecular constituents of these clouds.

RECENT attempts to interpret the intensity and distribution of interstellar molecules and their isotopic counterparts have led to some preliminary conclusions about the environment in which these molecules exist. And the predominance of organic species and their similarity to the products obtained in the synthesis of amino-acids in the study of the origin of life suggests a very close parallel between interstellar clouds and prebiotic chemistry. These are the directions in which the study of interstellar molecules is proceeding. The research is an interesting overlap of astronomy, physics, chemistry and biology and there are clearly exciting contributions to be made to all these fields. In this article I shall review present knowledge about interstellar clouds and indicate where the most promising future developments are likely to occur.

Early Discoveries

The chief breakthrough occurred in late 1968 and early 1969 with the discovery of NH_3, H_2O and H_2CO which occurred in rapid succession[1-3]. Until that time only simple diatomics were known to exist in the interstellar medium (Table 1) and it was thought that the environment was characterized by very low densities and large fluxes of ultraviolet radiation and cosmic rays—very difficult conditions for the formation and preservation of complex molecular species. The presence of dust grains, however, apparently plays a very important role in the molecular evolution of these clouds. The dust grains may provide the catalytic surfaces on which the molecules can form as well as the shielding necessary to protect the molecules from photo-dissociation. The extinction and reddening of starlight have been known for some time and the dust, which is presumed to be responsible for this, is thought to be in the form of carbon or silicates with a size of about 0.1 μm. Very little else is known about the composition of these particles; their temperatures are about 10 K and the ratio of the density of dust to that of hydrogen is about 10^{-12}. The dust seems to be located along the inner edges of the galactic spiral arms in regions of high density consisting chiefly of molecular hydrogen. The dust, hydrogen and molecular clouds usually appear in relatively dense condensations which are apparently in the process of collapsing into stars and planetary systems. Hence the evolution of the molecular clouds is intimately related to the evolution of the relatively thin interstellar hydrogen gas into dense hydrogen burning stars.

Detection of Formaldehyde

The most important molecule to have been found in interstellar clouds is probably formaldehyde. Eight microwave lines of this molecule have been found and the 6 cm absorption line, in particular, appears in a large number of galactic sources[4]. The formaldehyde seems to permeate the galaxy, showing a preference for dusty regions. The behaviour of this molecule in some of the nearby dust clouds is particularly interesting. The molecule was detected in absorption in these clouds against the faint 3 K microwave background radiation, a very peculiar state of affairs in which the molecule is being cooled or refrigerated below 3 K (ref. 5). The cooling occurs throughout these clouds and indicates a very general mechanism for pumping the formaldehyde. It was concluded that collisions with hydrogen molecules at a density of 10^3 cm^{-3} were responsible for the refrigeration[6]. In most of the other galactic sources the molecule seems to be in equilibrium with the 3 K microwave radiation. Presumably this is the result of the lower densities of 1 to 10 hydrogen atoms cm^{-3} in the interstellar medium.

Fig. 1 Orion nebula. (Photograph from the Mount Wilson and Palomar Observatories.)

One problem, as far as formaldehyde is concerned, is posed by the Orion nebula, a cloud about 10 light years across and 1,500 light years away (Fig. 1). It is usually the brightest object in the sky for molecular emission lines but the 6 cm absorption is quite weak[7]. The dark molecular cloud probably lies behind the bright emission nebula where the radio continuum originates. But why, then, does the formaldehyde not show up strongly in absorption against the 3 K background radiation? The formaldehyde is detected strongly in emission at 2 mm in the centre of the nebulae[8] and this emission requires a molecular hydrogen density of 10^5 molecules cm^{-3} in a region of size about 1 light year. The formaldehyde absorption indicates that the size of the molecular cloud is at least 10 light year extending chiefly to the south of the intense emission region. It would seem that somewhere in the cloud a strong absorption line could be produced at the density of 10^3 molecules cm^{-3} necessary for refrigerating the formaldehyde.

Hydroxyl Radicals

Studies of the distribution and excitation of the OH molecule have been carried on extensively since its discovery in 1963 (ref. 9). The molecule appears in absorption against a considerable number of galactic radio sources. Velocities of the clouds as measured in OH and H_2CO lines are similar and an approximate abundance ratio $OH/H_2CO \sim 30$ is obtained[4]. The abundance of hydrogen relative to formaldehyde is $H/H_2CO \sim 10^8$. These ratios vary considerably in different parts of the galaxy and almost all that can be said is that OH may be somewhat underabundant whereas the abundance of H_2CO is close to what would be expected from the atomic abundances of the constituent atoms.

In the nearby dust clouds the OH shows up in emission, thus indicating temperatures of about 10 K (ref. 10)—rather low by comparison with the typical hydrogen cloud temperature of 100 K; at the same time the formaldehyde is being cooled below 3 K. Presumably the same process heats the OH and cools the formaldehyde. In regions much higher in density than the 10^3 molecules cm^{-3} of the dust clouds, the OH is pumped into very intense maser emission. A similar situation occurs for the H_2O molecule. The sizes of these regions are quite small ($\sim$1 AU) and the amount of energy involved is quite large ($> 10^{30}$ erg s^{-1}). The densities required are about 10^8 cm^{-3} and indicate an object in the process of gravitational collapse. An interesting possibility is that the energy generated by the collapse is being radiated away by the maser emission process of the molecular cloud. In this case, through collisions with hydrogen molecules, the H_2O and OH are performing the important function of cooling the hydrogen cloud as it collapses into a protostar. The coincidence of the OH and H_2O maser in Orion with an infrared star in the densest part of the nebula strengthens this conclusion.

Carbon Monoxide

The CO molecule has a very stable triple bond which is difficult to dissociate and thus has a lifetime in an unprotected region of at least 1,000 yr compared with 30 yr for most other molecules[11]. The CO molecule is present in very large regions of most sources and apparently does not require the protection of dust grains[12]. This makes it an ideal molecule with which to map the structure of the Galaxy. It is also apparently very dense and generally opaque in the microwave line; this fact and the low dipole moment lead to the conclusion that it is a good indicator of the kinetic temperature in a cloud. By contrast the HCN molecule has a rather large dipole moment and will therefore have a stronger coupling to the radiation field[13]. The densities required to excite the CO molecule by collision are 2×10^3 hydrogen molecules cm^{-3} compared with 10^6 molecules cm^{-3} for HCN (ref. 14).

Isotopic Counterparts

The ^{13}C and ^{18}O isotopes of OH, H_2CO, CO and HCN are important for studying the extent to which nuclear burning processes have changed the isotopic abundances in various parts of the Galaxy. They also provide data about the extent

Table 1 Molecules Found in the Interstellar Medium

Year	Molecule	Symbol	Wavelength	Telescope	Initial discovery	
1937		CH	4300 Å	Mt Wilson 100 inch	Dunham	Mt Wilson
1940	Cyanogen	CN	3875 Å	Mt Wilson 100 inch	Adams	
1941		CH^+	3745–4233 Å	Mt Wilson 100 inch	Adams	
1963	Hydroxyl	OH	18, 6.3, 5.0 and 2.2 cm	Lincoln Lab 84 foot	MIT/Lincoln Lab	
1968	Ammonia	NH_3	1.3 cm	Hat Creek 20 foot	Berkeley	
1968	Water	H_2O	1.4 cm	Hat Creek 20 foot	Berkeley	
1969	Formaldehyde	H_2CO	6.2, 2.1 and 1 cm; 2.1 and 2.0 mm	NRAO 140 foot NRAO 36 foot	University of Virginia, NRAO, University of Maryland and University of Chicago	
1970	Carbon monoxide	CO	2.6 mm	NRAO 36 foot	Bell Labs	
1970	Cyanogen	CN	2.6 mm	NRAO 36 foot	Bell Labs	
1970	Hydrogen	H_2	1100 Å	UV rocket camera	NRL	
1970	Hydrogen cyanide	HCN	3.4 mm	NRAO 36 foot	University of Virginia and NRAO	
1970	X-ogen	?	3.4 mm	NRAO 36 foot	NRAO and University of Virginia	
1970	Cyano-acetylene	HC_3N	3.3 cm	NRAO 140 foot	NRAO	
1970	Methyl alcohol	CH_3OH	36 and 1 cm; 3 mm	NRAO 140 foot	Harvard	
1970	Formic acid	CHOOH	18 cm	NRAO 140 foot	University of Maryland and Harvard University	
1971	Carbon monosulphide	CS	2.0 mm	NRAO 36 foot	Bell Labs and Columbia University	
1971	Formamide	NH_2CHO	6.5 cm	NRAO 140 foot	University of Illinois	
1971	Silicon oxide	SiO	2.3 mm	NRAO 36 foot	Bell Labs and Columbia University	
1971	Carbonyl sulphide	OCS	2.7 mm	NRAO 36 foot	Bell Labs and Columbia University	
1971	Acetonitrile	CH_3CN	2.7 mm	NRAO 36 foot	Bell Labs and Columbia University	
1971	Isocyanic acid	HNCO	3.4 mm; 1.4 cm	NRAO 36 foot	University of Virginia and NRAO	
1971	Hydrogen isocyanide	HNC	3.3 mm	NRAO 36 foot	University of Virginia and NRAO	
1971	Methyl-acetylene	CH_3C_2H	3.5 mm	NRAO 36 foot	University of Virginia and NRAO	
1971	Acetaldehyde	CH_3CHO	28 cm	NRAO 140 foot	Harvard University	
1971	Thioformaldehyde	H_2CS	9.5 cm	Parkes 210 foot	CSIRO, Australia	

of line saturation in lines which have a high opacity. The terrestrial abundance of $^{12}C/^{13}C$ is 89 but the formaldehyde is found to have an anomalous abundance ratio for the galactic centre absorption line of $^{12}C/^{13}C=11$ (ref. 15). Recently the ^{18}O line of formaldehyde was detected in Sgr B2 and yielded an overabundance of ^{13}C relative to ^{18}O by a factor of two (ref. 16). This can be interpreted in terms of an abundance ratio $^{12}C/^{13}C$ of 45 and an opacity τ of 4.5. Interferometer observations of the source Sgr A give $^{12}C/^{13}C=25$ and $\tau=2$ (E. B. Fomalont and L. N. Weliachew, to be published).

There are at least two unidentified lines in the millimetre range around 90 GHz. The first is called X-ogen (ref. 17) and is possibly a line of HCO^+ (ref. 18). The second is tentatively identified as HNC based on a calculated frequency which falls close to the observed line (L. E. Snyder and D. Buhl, to be published). Neither of these molecules is stable in the terrestrial environment, but the interstellar medium may be a perfect place to manufacture and store such unusual species of radicals and ions. Undoubtedly there will be many more unidentified lines as receiver sensitivity increases, particularly in the millimetre range. The matching of a single line with a molecule is about 99 per cent reliable at the present density of microwave lines. Increased sensitivity will crowd the spectrum with lines and make it necessary to find several lines of a molecule before being certain of its identification. This can be done by searching for a second transition with different quantum numbers, detecting the ^{13}C isotope of the molecule or trying to resolve hyperfine splitting in the line in a source with a small Doppler width. Only two molecules, OH and H_2CO, have been identified by all these methods.

Larger Molecules

The larger organic molecules have generally only been found in the galactic centre source Sgr B2. This is probably due to the greater size of the region and possibly to the more efficient production of molecules in the galactic centre. The energy levels of these molecules are compressed because of the larger mass and a significant number of levels are thus populated, with the line frequency generally increasing at higher levels. The lines will usually be stronger at these higher levels and hence easier to detect. Several molecules (HNCO, OCS and CH_3CCH) have shown this tendency[19] and it therefore seems that the future detection of heavy molecules will come from higher level transitions with frequencies in the millimetre range. This is particularly true because the principal improvements in receiver sensitivity can be expected at these wavelengths[20]. The far infrared may be important for detecting molecular vibrational transitions as well as additional rotational transitions of light molecules such as H_2O.

The optical observations of the 1930s revealed several lines which were subsequently identified as the radicals CH, CH^+ and CN. Several interstellar diffuse bands have been observed, however, and particularly prominent is a line at 4430 Å (ref. 21). All attempts to identify these bands have failed. The porphyrin molecule has been suggested as a possible source of sixteen of the twenty-five bands[22] but the identification is quite controversial and needs further confirmation. It seems that the radio spectrum will also soon contain a considerable number of unidentified lines. The interstellar medium may very well contain molecules, radicals and ions with unusual structures not commonly encountered on Earth.

Origin of Life

Is there a connexion between the interstellar molecular clouds and the origin of life? It is difficult to establish a direct connexion, but the similarity of the organic molecules produced in laboratory experiments[23] to the molecular composition of interstellar clouds suggests a dominant direction in the chemical synthesis which proceeds despite the very different environment of the cool, low density interstellar clouds. These molecular clouds are believed to be located in regions where an important stage of evolution is taking place. The collapse and formation of a star from the gas in a diffuse nebula take place in a relatively short time scale and it is precisely at this time that the molecules appear in these condensing clouds. They probably provide the early atmospheres of planets which presumably form at the same time. Once the star evolves, the remainder of the condensing cloud is blown away and any molecules left will probably be dissociated. The Earth is assumed to have lost its early hydrogen rich atmosphere so most of the primordial gas will also be lost.

Some extra-terrestrial organic material does, however, fall on the Earth. The discovery of abiological amino-acids in the Murchison meteorite[24] indicates that complex organic material from other parts of the solar system often adds very small amounts of unusual amino-acids to the Earth's biosphere. On a larger scale the collision of a comet with the Earth may add considerable amounts of primordial organic molecules. Such collisions were probably relatively frequent during the first 10^9 years of the Earth's history and comets are thought to be large frozen samples of the original solar nebulae which orbited the Sun at considerable distances. Several develop highly elliptical orbits which bring a few large comets each year into the vicinity of the Sun and the Earth. One can only conclude that, although the collision of a comet with the Earth may have been a relatively frequent event, it is uncertain whether sufficient amounts of organic material would have been added to influence the origin of life or affect its subsequent evolution.

The important parallels appear to be between the formation of interstellar molecules and the synthesis of amino-acids in prebiological chemistry experiments. It is here that the key to the evolution of interstellar molecular clouds lies.

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South Polar and Equatorial Differences in Central Peaked Martian Craters

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Central peaks in Martian craters in the south polar region occur more frequently than their equatorial counterparts and the peak frequency statistics and crater morphologies imply that preferential peak production has taken place.

We report the results of a preliminary study of the distribution of central peaked Martian craters based on photographs taken by Mariner 6 and Mariner 7; this study provides information about the origin of these craters and about the geological processes occurring on the surface of Mars. By comparing our results with statistics of central peaks in lunar craters[1], we can deduce whether or not similar crater forming and eroding processes have taken place on Mars and on the Moon.

Theories of the origin of central peaks in craters include formation by impact, volcanic activity, permafrost (pingos) and uplift following isostatic compensation. Mechanisms for the erosion of such peaks include meteoritic bombardment, a gradual relaxation of the structure through creep and—in the case of Mars—the action of wind and water (ice) especially through freeze–thaw cycles.

Identification and Measurement

Regions of low solar illumination were studied so that the maximum number of central peaks could be detected. For Mariner 6 and 7 the Martian equatorial region from about latitudes 10° to 20° S (frames 6N19, 21, 23 of Deucalionis Regio) and the south polar region at $\gtrsim 70°$ S (frames 7N11, 13, 15, 17, 19) were suitably illuminated. These were divided into regions of comparable solar illumination along lines 10°, 20° and 30° from the terminator and separate crater peak investigations were carried out within each of these regions. In this way comparable lower limits in elevations (or slopes) could be expected in features seen in corresponding equatorial and polar areas.

Although equatorial crater identification was hindered by resolution limits and lack of contrast, observations in the south polar areas were more difficult because of partial rim destruction, surface obscurations and apparently rough terrain.

Crater peak recognition was more difficult than crater identification because peaks are smaller than craters, peak forms are more diverse than crater forms, and peaks are more adversely affected by surface contrast deficiencies. Peaks were required to exhibit a bright region in the direction of the Sun and a dark region in the opposite direction, to give the impression of positive topographic relief. This requirement minimizes the chance of mistaking possible frost accumulations[2] on crater floors for central peaks. In all but a very few instances unambiguous albedo variations suggesting peaks were discernible. The few questionable cases do not substantially affect the data or the conclusions drawn from them.

Many examples of Martian central peaks can be seen in the orthographic projection of Mariner frame 7N19 (Fig. 1). In the upper left part of Fig. 1 a massive dome formation of diameter ~150 km with a central peaked crater can be seen. The crater diameter is ~50 km and the central peak is ~20 km wide. Such a broad central peak is atypical of those seen on the Moon. The apparent partial remains of a large ring structure (~800 km in diameter) can also be seen in the central

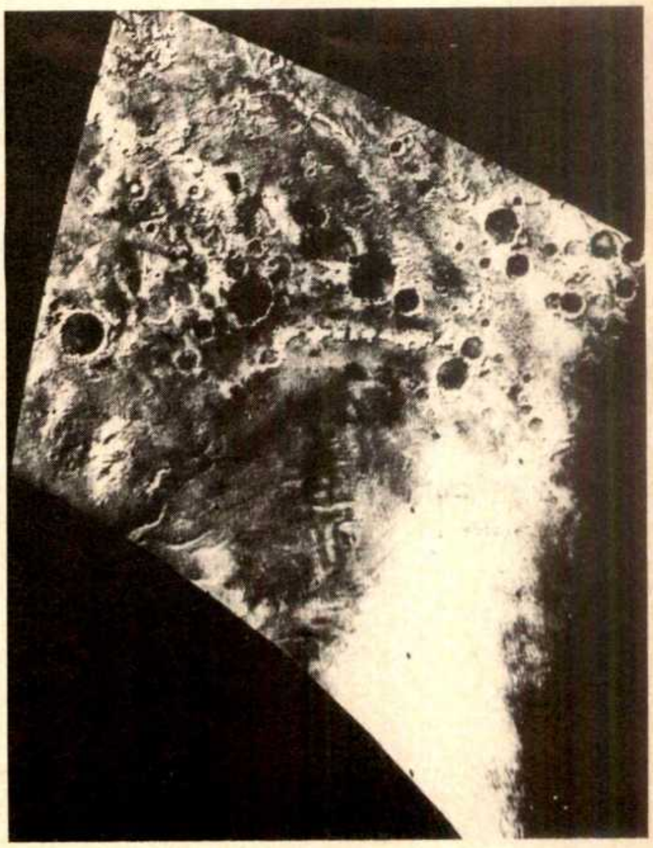

Fig. 1 Orthographic projection of Mariner frame 7N19 showing numerous craters with central peaks. In the upper left, a massive dome formation with a broad central peaked crater can be seen. In the centre, the partial remains of a large apparent ring structure can be identified.

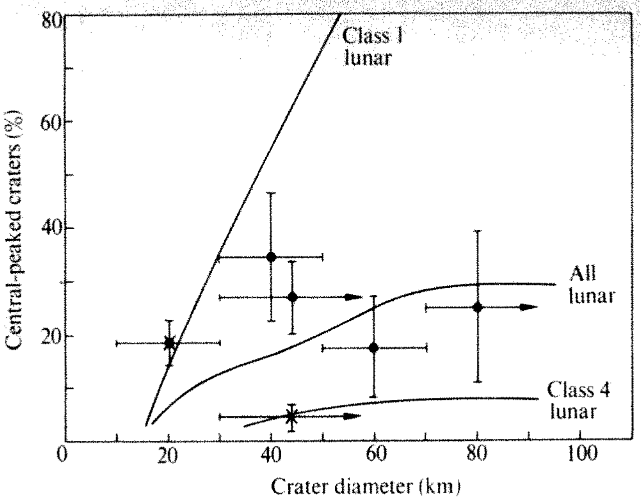

Fig. 2 Percentage of craters with central peaks as a function of crater diameter for Martian south polar and equatorial craters and lunar craters[1] in various stages of preservation. ×, Equatorial craters; ●, polar craters.

portion of Fig. 1. If this arc does indeed represent what was once a ring structure it would suggest that Mars, like the Moon, experienced catastrophic imbrium-like impact events early in its history.

Crater diameters were measured between rim summits along the direction of least foreshortening and account was taken of the variation of scale within the frames. Cumulative crater size-frequency distributions were compiled from the crater counts and diameter measurements; these distributions are in agreement with those previously observed[3] and show no significant variation with solar illumination angle within the range 0° to 30°.

Central Peak Statistics

The smallest crater in which a peak was clearly resolvable had a diameter of ~10 km. This was also the lower limit of crater diameters included in the statistical study of lunar peaked craters[1]. In the south polar region, thirty-nine craters with central peaks were observed out of a total of 179 craters with diameter >10 km, and in the equatorial region 28 craters with central peaks were found out of a total of 203. The crater counts are listed in Table 1 as a function of crater diameter.

Table 1 South Polar and Equatorial Statistics of Central Peaked Martian Craters

	Crater diameter (km)	No. of peaks	No. of craters	% of peaks
South polar	11–30	20	108	18.5
	31–50	11	32	34.4
	51–70	4	23	17.4
	>71	4	16	25.0
Equatorial	11–30	25	134	18.6
	>31	3	69	4.3

The proportions of all craters with central peaks in the south polar and equatorial regions of Mars are 22±4% and 14±3%, respectively. The percentage in the equatorial region is consistent with interpretations[4] of the Mariner 4 photographs at comparable latitudes—central peaks were reported in ~11% of the craters of diameter >10 km. But the low resolution of the Mariner 4 rendered both peak and crater identification much less reliable.

The Martian peak frequency is substantially greater than the 7% reported[1] for all lunar craters in the same size range. These percentages for the Mariner 6 and 7 data are shown in Fig. 2, as a function of crater diameter, together with the percentages determined for lunar craters[1]. There is a significant difference between relative frequency of south polar and equatorial peaked craters. For craters with diameter $D > 30$ km the frequency of central peaks in the polar region is six times that in the equatorial region and no central peaks were identified in the equatorial region in craters larger than 40 km in diameter. The fact that these frequencies each differ from a common mean by more than two standard deviations implies an important difference in either the origin or evolution of peaked craters in the south polar and equatorial regions. In this same diameter range the south polar frequency is in qualitative agreement with the frequency for all lunar craters. The equatorial frequency is four standard deviations lower than that of the combined lunar group but approximates that of class 4 lunar craters which are severely degraded and presumably among the oldest. There is a suggestion that the proportion of polar central peaks in the interval $30 < D < 50$ km exceeds that of the combined lunar craters. For craters with $D < 30$ km the frequencies of central peaks in the Martian polar and equatorial regions are nearly identical. Also, the frequencies in this diameter range are comparable with central peak frequencies in class 1 lunar craters but exceed by almost three standard deviations the frequencies in all lunar craters. Class 1 lunar craters have very sharp and complete rims and are presumably the youngest[1].

Excess and Agreement

To understand the south polar excess in the frequency of central peaked craters for $D > 30$ km and the agreement in the frequency statistics for $D < 30$ km we must consider the overall morphology of Martian craters. Two extreme types of Martian craters have been recognized[3], small bowl-shaped ones and large flat-bottomed ones. The bowl-shaped craters predominate at diameters <15 km and show little evidence of modification, whereas flat-bottomed craters predominate at greater diameters and are significantly modified, with greatly subdued rims and generally unrecognizable secondary craters and ejecta blankets. The small bowl-shaped craters are clearly younger because they would have been degraded along with the ejecta blankets and ray systems of the larger craters if they had been created at the same time. And the absence of large fresh craters suggests either that the distribution of objects incident on Mars was deficient in large bodies compared with that of objects incident on the Moon, or that erosion is more efficient on Mars.

These descriptions of Martian crater morphology and the assumption that the origin of Martian central peaks is similar to that of lunar rebound peaks[5] imply that the central peak frequency in craters of diameter >30 km should be small and in rough agreement with that of the degraded (class 4) lunar craters. Furthermore, the central peak frequency in the smaller craters ($D < 30$ km) should be comparable with that of the fresh (class 1) lunar craters. It can be seen from Fig. 2 that these conclusions are in agreement with the equatorial statistics and the south polar statistics for $D < 30$ km. For $D > 30$ km, however, the central peak frequency in the south polar region is significantly greater than that in the equatorial region and in class 4 lunar craters. This could suggest preferential peak formation in the south polar region.

A possible alternative explanation of the polar–equatorial differences in central peak crater statistics is preferential peak erosion in the equatorial region. This is consistent with the rough agreement between central peak frequency in south polar craters and all lunar craters but it is inconsistent with the qualitative observation that the Martian craters generally appear more degraded than lunar craters[3]. There is no evidence, however, that erosion has taken place preferentially in the equatorial region because the overall crater morphology is similar in these regions (in particular, the rims of the large craters appear to be equally subdued) and the population indices of the cumulative crater size frequency distributions are nearly the same in this size range ($D > 30$ km) for both regions. We therefore conclude that preferential central peak formation has occurred in the south polar region.

From the limited coverage by Mariner 6 and 7 we cannot determine whether this preferential central peak production is a latitude effect or simply a regional variation. The similarity of the peak frequencies observed in Mariners 4 and 6 at widely separated equatorial regions would, however, suggest a latitude variation. If the phenomenon is latitude-dependent pingo formation might be the source of the peaks because Martian permafrost may be confined to polar latitudes[6]. But if the phenomenon is simply a regional variation, it may be explicable in terms of volcanism or other mechanisms.

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Haemoglobin Constant Spring—A Chain Termination Mutant?

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Haemoglobin Constant Spring is an unusual variant which comprises only 1–2% of the total haemoglobin in heterozygotes. It has α-chains which are 172 residues long instead of the normal 141, and when it is inherited together with an α-thalassaemia gene it gives rise to haemoglobin H disease.

MOST human haemoglobin variants result from single amino-acid substitutions in one of the globin chains. Normal adult haemoglobin is made up of haemoglobin A (Hb A) which consists of 2α and 2β-chains ($\alpha_2\beta_2$) and haemoglobin A_2, the normal minor component, which has the formula $\alpha_2\delta_2$. The α-chains contain 141 amino-acids while the non-α-chains are 146 residues long. Each of the reported substitutions has been consistent with a single base change in the DNA which codes for the affected chain[1]. In a few other variants (such as Hbs Freiburg and Gun Hill) one or more amino-acids have been deleted, probably during intragenic crossing over[2,3]. Finally, in several abnormal haemoglobins (the haemoglobin Lepores and anti-Lepores) normal α-chains are combined with chains made up of the N-terminal residues of the δ-chain combined with the C-terminal residues of the β-chain or vice versa These composite δβ or βδ-chains are also 146 residues long and have probably arisen by unequal crossing over between the closely linked δ and β-loci[4].

We report here a different type of human haemoglobin variant which has an additional thirty-one residues at the C-terminal end of the α-chain, apparently due to a type of mutation which differs from those previously responsible for the production of haemoglobin variants.

The new variant (Hb CS) was discovered in Constant Spring, Jamaica, in a large Chinese family in which three children have haemoglobin H disease, a disorder which is characterized by a moderately severe haemolytic anaemia associated with the presence of 5–20% Hb H (ref. 5) and variable amounts of haemoglobin Bart's. Hb H consists of 4 β-chains (β_4) while Hb Bart's is γ_4; both result from a reduced rate of α-chain production (α-thalassaemia) leading to the accumulation of excess β and γ-chains in the cell[6]. Haemoglobin H disease usually follows the inheritance of two α-thalassaemia genes, severe and mild, designated α-thalassaemia 1 and 2 (ref. 7). The α-thalassaemia 1 gene results in a complete suppression of α-chain synthesis[8], whereas the α-thalassaemia 2 gene leads to a reduced production of α-chains. Usually in haemoglobin H disease the haemoglobin consists of A and H only, but in this family the affected children carried about 2% of slowly migrating haemoglobin (Hb CS) which resolved into two bands on starch gel electrophoresis[9]. About 1% of Hb CS was found in the children's father and several siblings, while the mother carried the α-thalassaemia 1 gene. The relative proportions of the two Hb CS components (Hb CS1 and Hb CS2) varied between samples but in fresh red cell lysates the more anodal fraction at *p*H 8.5 (Hb CS1) always exceeded that of Hb CS2; occasionally Hb CS1 was the only fraction observed. Full genetic and clinical details of this family[9] indicate that the Hb CS gene can interact with the α-thalassaemia 1 gene to produce haemoglobin H disease. For this reason we have examined both the structure and rate of synthesis of Hb CS.

Structure

Pure Hb CS was prepared from the blood of a child with haemoglobin H disease and Hb CS. Haemolysates were made in a standard way[10] and cleared by centrifugation at 20,000*g* for 30 min. A sample containing about 2 g of haemoglobin was dialysed against phosphate buffer[11], *p*H 7.12, and applied to a 2 × 30 cm 'Amberlite IRC 50' column at 4° C. After elution

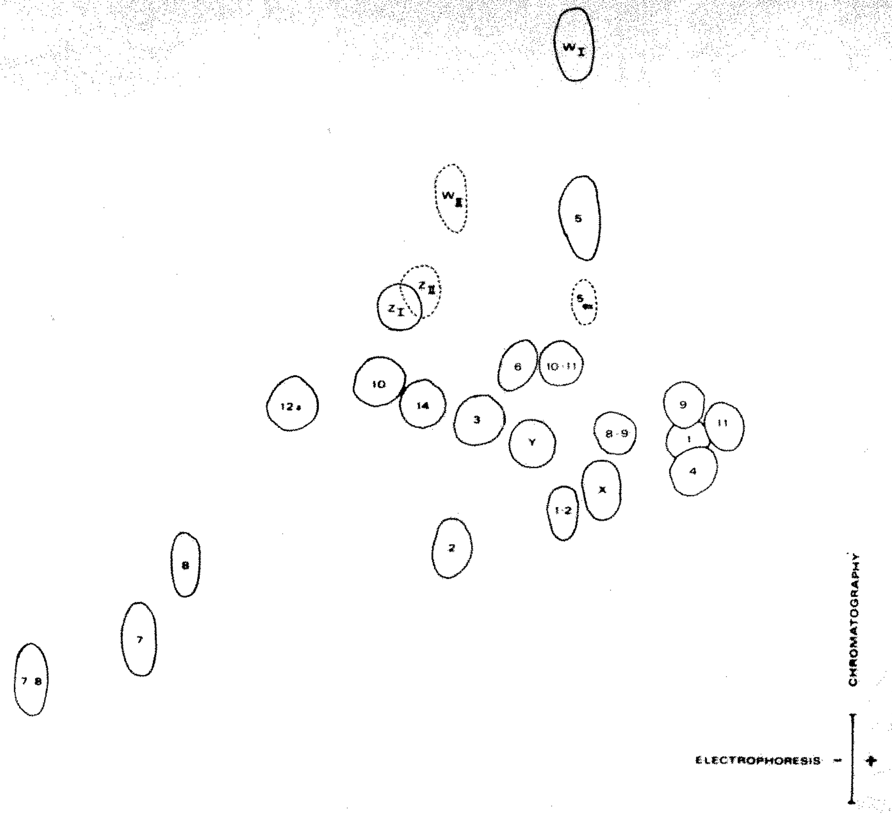

Fig. 1 Superimposed tracings of fingerprints of tryptic digests of the α^{CS1} and α^{CS2}-chains. The two peptides derived from the C-terminal end of the α^{CS2}-chain are shown as broken circles.

of haemoglobins H and Bart's at 4° C, the column was allowed to equilibrate at 25° C and haemoglobins A and A_2 were then eluted. Hb CS remained as a tight band at the top of the column and was eluted with the same phosphate buffer made 0.3 M in NaCl. Hb CS prepared in this way was contaminated with less than 10% Hb A on starch gel electrophoresis. The yield of Hb CS1 was always greater than Hb CS2 when prepared in these conditions.

Globin prepared from the purified Hb CS fraction by acid-acetone precipitation was separated into its constituent chains by chromatography on CM-cellulose in 8 M urea/2-mercaptoethanol buffers as described previously[12]. Two abnormal α-chain components (α^{CS1} and α^{CS2}) were observed in proportions corresponding to the two Hb CS fractions seen on starch gel electrophoresis, while the β-chains were identical to those of haemoglobin A. Fingerprints[12] prepared from trypsin digests of the aminoethylated derivatives of the two abnormal α-chain components (Fig. 1) showed that all the peptides normally found in α^A-chain digests were present and had the expected amino-acid compositions. In addition there were four extra peptides (W, X, Y and Z) present in both the α^{CS1} and α^{CS2} fractions, the compositions of which (Fig. 2) did not correspond with any tryptic peptides from human α, β, γ or δ-chains.

Studies on the fragments obtained from the α^{CS1}-chain by cyanogen bromide cleavage indicated that the additional peptide material extended beyond the normal C-terminal residue of the α^A-chain (141 Arg), and this was confirmed by the finding that the free arginine derived from Arg 141, and normally present on fingerprints of chymotrypsin digests of the α^A-chain, was missing in digests of α^{CS1}-chain, and had been replaced by three new arginine-positive peptides with compositions corresponding to residues 141–154, 155–160 and 166–168 of the α^{CS1}-chain (Fig. 2).

The additional trypsin peptides account for an extra thirty-one residues so that in Hb CS the α^{CS1}-chain is 172 residues long and has a molecular weight of 18,500. This agrees approximately with the value of about 20,000 found for the slower of the two bands observed on SDS-gel electrophoresis[13] of Hb CS globin. Normal Hb A globin gave only one band with a mobility identical to that of the faster (that is, the β-chain) of the two bands from Hb CS globin. The amino-acid sequence of the extra residues of the two α^{CS}-chains has been determined and is shown in Fig. 2. The difference between the two α-components lies in the absence of the C-terminal tripeptide Val.Phe.Glu in the α^{CS2}-chain, accounting for the two related peptides W_I and W_{II} found in the trypsin digests of the α^{CS1} and α^{CS2}-chains respectively. Peptides Z_I and Z_{II} presumably resulted from a weak trypsin split at the Arg-Pro bond at position 166–167. Since some conversion of α^{CS1} to α^{CS2} can take place in haemolysates in certain conditions (for example, on storage) it seems likely that the α^{CS2}-chain is normally derived from the α^{CS1}-chain, probably by the action of intracellular proteolytic enzymes.

Biosynthesis

The fact that α^{CS1} can be converted to α^{CS2} suggested that the low amounts (1–2%) of the Hb CS in the peripheral blood of our subjects might not be representative of the true rate of synthesis of the α^{CS}-chain. The relative rates of synthesis of haemoglobins A and CS were therefore examined in labelling experiments. Washed peripheral blood cells, containing from 5–10% reticulocytes, from the individuals heterozygous for Hb CS alone or for Hb CS and α-thalassaemia 1 were incubated with ^{3}H-leucine or ^{3}H-arginine for 5 min to 2 h (ref. 10). Cells were washed, lysed and the total "globin" precipitated by the acid-acetone method. The distribution of radioactivity in the globin chains after separation by CM-cellulose chromatography in 8 M urea was then determined (Table 1). In the samples from individuals doubly heterozygous for Hb CS and α-thalassaemia 1 the total radioactivity incorporated into the β and γ-chains exceeded that incorporated into the combined α^A and α^{CS}-chains by a factor of approximately 2 to 1, a ratio similar to that found in haemoglobin H disease[6]. Furthermore, the specific activity of the β-chain exceeded that of the α-chains, indicating that there is less unlabelled β-chain present than would be expected from its rate of synthesis. These findings, caused because excess β-chains precipitate in the red cell and are removed in the circulation, are also typical of haemoglobin H disease[6]. In a further experiment reticulocytes from one of the individuals heterozygous for α-thalassaemia 1 and Hb CS

Table 1 Radioactivity Incorporated into Globin Chains after Incubation of Reticulocytes of an Individual heterozygous for α-Thalassaemia 1 and Hb CS

Experiment	Isotope	Incubation time (min)	Total c.p.m. $\gamma+\beta$	Total c.p.m. α^{A}	Total c.p.m. α^{CS1}	Ratio $\alpha/\beta+\gamma$
1	^{3}H-leucine	5	10,446	5,181	56	0.50
	^{3}H-leucine	120	154,546	64,704	751	0.42
2	^{3}H-arginine	15	2,850	1,436	14	0.51

were incubated with ^{3}H-leucine for 1 h and haemoglobins H, A and CS separated by 'Amberlite' chromatography and the relative specific activities of the whole haemoglobins and their constituent globin chains determined. In the haemoglobin A fraction the specific activity of the α-chain exceeded that of the β-chain, indicating that there is a large pool of β-chains in these red cells and that newly made α-chains combine with β-chains from this pool. This too is typical of haemoglobin H disease[6].

In all these experiments very little radioactivity was incorporated into the α^{CS1} and α^{CS2}-chains and their specific activities were considerably less than that of the α^{A}-chain. These observations, consistent for incubation times of 5 min to 2 h, indicate that the α^{CS}-chain has a low turnover rate and is not destroyed rapidly after synthesis. This was confirmed by determining the specific activities of the arginine-containing peptides of the α^{A} and α^{CS}-chains after incubating the cells of an individual heterozygous for α-thalassaemia 1 and Hb CS with ^{3}H-arginine for 15 min (Table 2). The lower specific activity of the α^{CS}-chain compared with α^{A}-chain suggests that either the ability to synthesize the α^{CS}-chain diminishes as the red cell matures, rather like the δ-chain of Hb A_2 (ref. 14), or that it is assembled more slowly than the α^{A}-chain. The data shown in Table 2 are not compatible with the latter possibility, however, since there is no significant difference between the specific activities of the N-terminal and C-terminal arginine-containing peptides of the α^{CS}-chain after 15 min of incubation with ^{3}H-arginine. If a reduced rate of assembly were responsible for a twenty-fold reduction in the rate of α^{CS}-chain production, compared with that of the α^{A}-chain, it seems unlikely that it would have been uniformly labelled after only 15 min, since it takes about 9 min at 37° C to uniformly label normal α^{A}-chains[15].

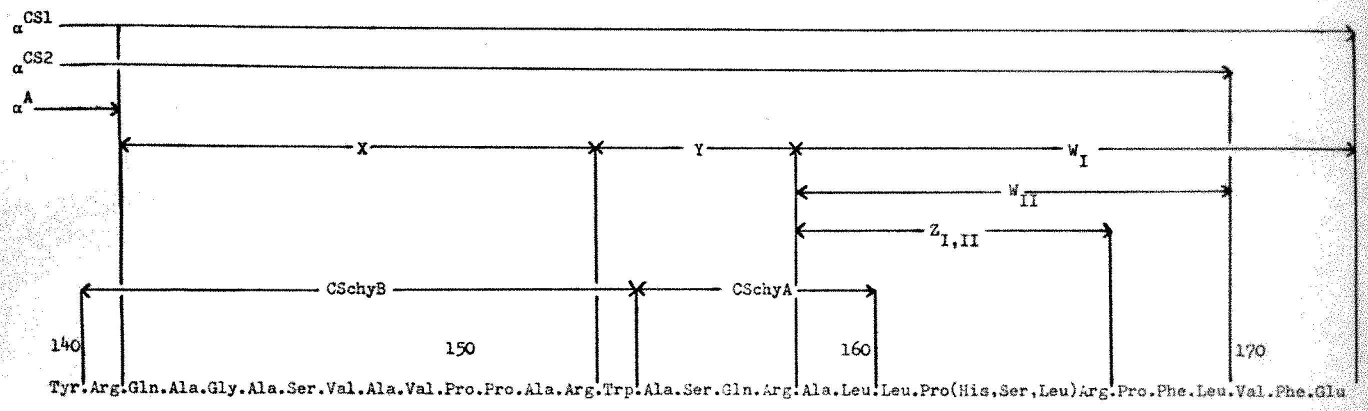
α^{CS1}
α^{CS2}
α^{A}
X
Y
W_{I}
W_{II}
$Z_{I,II}$
CSchyB
CSchyA
140
150
160
170
Tyr.Arg.Gln.Ala.Gly.Ala.Ser.Val.Ala.Val.Pro.Pro.Ala.Arg.Trp.Ala.Ser.Gln.Arg.Ala.Leu.Leu.Pro(His,Ser,Leu)Arg.Pro.Phe.Leu.Val.Phe.Glu

Fig. 2 Amino-acid sequences of the α^{CS1} and α^{CS2}-chains, showing some of the peptides isolated and used in the sequence determination. Full details of the determination of the sequences of α^{CS1} and α^{CS2} will be published elsewhere.

Table 2 Specific Activities of α^{CS1}-Chain Peptides and α^{A}-Chain Peptides after Incubation of Reticulocytes from an Individual heterozygous for α-Thalassaemia 1 and Hb CS for 15 min at 37° C

Peptide	Specific activity (c.p.m. ^{3}H-Arg/μmol ^{12}C-Arg)
α^{A} 4	1,810
α^{A} 10	2,020
α^{A} 14	1,880
α^{CS1} 4	304
α^{CS1} 10	366
α^{CS1} 14	360
α^{CS1} X	283
α^{CS1} Y	279

The ratio of α to β-chain production in the parent heterozygous for Hb CS alone was 1.05/1, indicating no gross imbalance of globin chain production. This finding is similar to that reported for α-thalassaemia 2 carriers[16]. The α/β ratio in the other parent, heterozygous for α-thalassaemia 1, was 0.56, very similar to that reported for α-thalassaemia 1 heterozygotes[16].

The structural and biosynthetic data indicate that Hb CS is a variant with an elongated α-chain and that as the red cell matures the ability to produce α^{CS}-chains declines more rapidly than the ability to produce α^{A}-chains. Furthermore, the associated genetic findings[9] suggest that the *Hb CS* gene interacts with an α-thalassaemia 1 gene to produce haemoglobin H disease. In this respect the *Hb CS* gene behaves like the α-thalassaemia 2 gene, since Hb H is not normally found in the blood of individuals heterozygous for either the α-thalassaemia 1 or α-thalassaemia 2 genes alone, but only in persons doubly heterozygous for α-thalassaemia 1 and α-thalassaemia 2.

The Molecular Defect

There are several possible explanations for these observations. The simplest is that α^{CS} has arisen from a mutation of an α-chain gene terminating codon (UAA or UAG) to a glutamine codon (CAA or CAG) by a single base mutation or possibly by a deletion of the entire codon. This presupposes that the α-chain messenger RNA is longer than required to code for the 141 amino-acids normally present in the α^{A}-chain, and that in the absence of the normal terminating codon the message is read until another terminating codon is reached, so producing an α-chain with thirty-one extra residues attached to the C-terminal end. It is not clear from this model why this variant should be produced in such small amounts but it is unlikely to be due to a reduced rate of translation or termination of the additional piece of messenger RNA: the data on the rate of uniform labelling of the α^{CS}-chain are not consistent with this explanation. The production of small amounts of Hb CS could be explained by a terminating codon mutation if one assumes that the mutation is in a minor α-chain locus which normally directs the synthesis of about 1% of the total α-chain. Evidence for such a locus has been obtained in the great apes[17]. However, this mechanism would not explain the overall deficit of normal α^A-chains which accompanies Hb CS. Another explanation is that there is no further terminating codon after the normal termination point in the α-chain mRNA and that the small amounts produced result from a "pile up" of α^{CS}-chains which are released slowly from the ribosomes by non-specific proteolysis rather than by the normal process of chain termination. Again the data on the chain assembly time are not consistent with this model. Thus although a mutation in a chain terminating codon is perhaps the most likely, and attractive, explanation for the existence of Hb CS, it does not readily account for the small amounts produced or its relatively low rate of production in reticulocytes.

There are, of course, other possible explanations for the production of Hb CS, although none of them adequately explain both the small amounts produced and the relatively reduced rate of production in reticulocytes. Suppressor mutations have not been reported in mammalian cells but there is no reason why they should not exist.

A low efficiency suppressor of chain termination could explain the formation of small amounts of Hb CS although perhaps not its reduced rate of synthesis. A mutation in a minor glutamine transfer RNA, enabling it to recognize the chain terminating codon and insert glutamine, could account for the elongated α^{CS}-chain. A general suppressor of this type would be expected to suppress all appropriate chain terminating codons in other messenger RNAs. In most cases 1% of gene product would be undetected and even in the case of haemoglobin, which makes up 95% of the total protein in the red cell, only the fortuitous occurrence of charged residues in the extra piece enables the small quantities of Hb CS to be distinguished from haemoglobin A. We have no evidence of abnormal β-chains in these cells, but 1% of a β-chain variant with the same electrophoretic properties as Hb A would be very difficult to identify.

Finally, it is possible that the extra residues at the end of the α^{CS}-chain have arisen by unequal crossing over in a similar way to the Lepore haemoglobins, although the extra piece bears no resemblance to any other human globin chain. Possibly the cross over could have occurred with another gene altogether or with a globin chain gene which is out of phase as a result of the abnormal cross over. It has been suggested that thalassaemia-like disorders could result from crossing over between minor α-chain loci of the kind found in the great apes and the major α-chain loci[17], but the length and composition of the extra piece make such a mechanism an unlikely basis for the production of Hb CS.

Recently another human haemoglobin variant with an elongated chain, in this case the β-chain, has been described[18]. In this variant the structure of the extra piece is not compatible with a termination codon mutation suggesting that such variants can indeed arise by a variety of mechanisms.

Whatever the explanation for the production of the small amounts of the elongated α^{CS}-chain it seems likely that the messenger RNA for normal α^A-chains is longer than that required to code simply for 141 amino-acid residues. This would agree with the recent finding that the molecular weight of rabbit haemoglobin messenger RNA, as determined by SDS-gel electrophoresis and ultracentrifugation, appears to be some 50% greater than that required for an RNA of sufficient length to code for the sequence of the α and β-chains alone[19,20]. Our results suggest that haemoglobin α-chain messenger RNA has additional genetic material which extends for almost 100 nucleotides beyond the normal chain terminating codon.

Genetics and Distribution

The structure of Hb CS also has important implications for the understanding of the genetic control of the α-chain of human haemoglobin. There is conflicting evidence as to whether there are one or more structural loci directing α-chain synthesis, and, indeed, the situation may differ between populations[21,22]. There is now good evidence that the α-thalassaemia 1 gene is associated with a total deficiency of α-chain production directed by the affected chromosome[8]. The three individuals heterozygous for both α-thalassaemia 1 and Hb CS have haemoglobins A, H and CS. Thus the synthesis of both α^A and α^{CS}-chains must be directed by one chromosome and, unless the suppressor hypothesis is correct, this means that there are multiple α-chain loci on each chromosome, at least in the Chinese population in Jamaica. Furthermore, the similar mode of expression of the Hb CS and the α-thalassaemia 2 genes lends support to the suggestion that the α-thalassaemias are caused by total suppression of the α-chain production at either one (in the case of α-thalassaemia 2) or both genes (in the case of α-thalassaemia 1), of a duplicate α-chain-gene complex[23].

There have been reports in the past three years, from both Greece[24] and Thailand[25], of a minor haemoglobin variant being found in association with haemoglobin H disease. The Thai variant has an abnormal α-chain and its electrophoretic properties are very similar to Hb CS[25]. Furthermore, recent observations in Hong Kong and Malaya (Drs Lie-Injo Luan Eng and D. Todd, personal communications) suggest that a haemoglobin similar to Hb CS is frequently observed in patients with haemoglobin H disease. It appears therefore that these Hb CS-like variants often occur in association with haemoglobin H disease and it seems unlikely that this is coincidental. A more probable explanation is that the α^{CS} gene complex behaves very much like an α-thalassaemia 2 locus, and is thus subjected to selection factors similar to those which have been responsible for maintaining the α-thalassaemia genes at a high level in these populations.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Black Holes and Binary Stars

Gibbons and Hawking[1] have suggested that a number of spectroscopic binaries contain black holes. The formation of a black hole in a binary system would be accompanied by a sudden loss of mass from the system, and they believe that this mass loss could convert an initially circular orbit into an appreciably elliptical one. Only masses greater than 1.4 $M_\odot$ can collapse into black holes, and normal double-line spectroscopic binaries cannot contain black holes, so Gibbons and Hawking investigate those single-line spectroscopic binaries listed in the *Sixth Catalogue*[2] for which they estimate that each component has a mass greater than 1.4 $M_\odot$. There are only seven such systems, three of which have orbital eccentricities greater than 0.08. On the other hand, there are 55 double-line systems in which both components are more massive than 1.4 $M_\odot$, and eight of these have orbital eccentricities greater than 0.08. Comparing the relative numbers of eccentric and circular orbits in these two rather small samples, Gibbons and Hawking conclude that there is an excessive number of eccentric orbits among single-line spectroscopic binaries, and that the formation of black holes in some of the systems may have produced this excess. Specifically, they suggest that HD 176318, HD 184035 (201 G Sgr), and HD 194495 may contain black holes.

There are two implicit assumptions in this argument that, in our opinion, are not justified. The first is that the true frequency distribution of orbital eccentricities is similar to their observed distribution, and the second is that the observed frequency distribution of orbital eccentricities is expected to be the same for single-line and double-line spectroscopic binaries. There are three reasons for questioning their assumptions. (1) An orbit that is in fact circular may appear to have a small eccentricity introduced in the process of calculation of orbital elements by a fortuitous distribution of observational errors. (2) Some spectroscopic binaries that are also eclipsing binaries have velocity curves from which appreciable orbital eccentricities would be deduced were it not that the light curves clearly show these eccentricities to be spurious. Most of these systems are single-line binaries. (3) The probability of discovery of a spectroscopic binary depends on the orbital elements, in particular the eccentricity. Selection effects resulting from this dependence are strong enough to modify appreciably the observed distribution of eccentricities, and they act differently for single-line and double-line spectroscopic binaries.

Although Gibbons and Hawking restrict their discussion to orbital eccentricities greater than 0.08, the orbital eccentricity of HD 184035 is only 0.09. The period of this system is uncertain because only a few cycles have been observed[3] and therefore the other orbital elements are probably more uncertain than is usual. The eccentricity, in particular, may be of the spurious kind defined in (1). Lucy and Sweeney[4] have recently recomputed the elements of several spectroscopic binaries and tried to set up a test of the reality of small eccentricities. For HD 184035 they find $e = 0.049$ and judge that the orbit is essentially circular. Their result at least makes it doubtful whether the orbital eccentricity is large enough to suggest that there is anything unusual about the invisible component.

The distortion of velocity curves mentioned in (2), was frequently commented on by Struve[5]. He pointed out that there is an excessive proportion of observed values of the longitude of periastron, ω, in the interval 0° to 90°. Savedoff[6] showed that the values of $e \cos \omega$ obtained from light curves and velocity curves of the same eclipsing systems frequently differ—especially for binaries with periods less than 5 days that contain primary components of spectral type A5 or earlier. The detailed distribution of ω has been discussed most recently by Batten and Ovenden[7]. The distortion is often most pronounced in the Algol-type systems which contain a primary component of spectral type late B and a G-type or K-type sub-giant with a spectrum which is usually invisible except during the eclipse of the brighter star. For example, "eccentricities" of up to 0.5 and values of ω of about 45° have been found from velocity curves of U Cephei, although its light curve shows that $e \cos \omega$ must be close to zero. If a system of this type were not eclipsing, its secondary spectrum could not be detected. The distortion of the velocity curve is usually ascribed to phenomena within the orbital plane, but an Algol-type system that is oriented so as just to fail to display eclipses to a terrestrial observer may still have an appreciably distorted velocity curve. The periods, velocity ranges, and spectra of HD 176318 and HD 194495 are all consistent with the hypothesis that these systems are of this type.

Selection effects, mentioned in (3), are different for single-line and double-line binaries because a single-line binary is discovered by the variation of its velocity but a double-line binary is detected if its component spectra can be resolved. The probability of discovery depends on the elements e and ω, and on the orbital period, P. In addition, the discovery of a single-line binary depends on the ratio of the half-range of velocity, K, to the minimum detectable velocity variation Δ, while that of a double-line binary depends on the ratio of the sum of the half-ranges of each component, $K_1 + K_2$, to the minimum line separation, Δ', needed to resolve the spectra. An extensive, unpublished investigation by Ovenden and Olowin shows that over a wide range of values of K/Δ or $(K_1 + K_2)/\Delta'$, the discovery probability of double-line binaries decreases more rapidly with increasing orbital eccentricity than does that of single-line binaries. This selection effect therefore acts in the right sense to account for the different proportions of eccentric orbits, discovered by Gibbons and Hawking, among the two kinds of binaries. Although its total effect in a large sample should not be large, it might well affect small samples such as they discussed. Scott[8] has also studied the observed distribution of eccentricities on the basis of the catalogue compiled by Moore and Neubauer[9]. She calculated the observed distributions that would be produced by observational selection acting on a variety of assumed "true" distributions. When K/Δ is small, close to 2, none of the calculated distributions differ significantly from the observed distribution.

We are puzzled by the suggestion that image intensifiers be used in an attempt to detect the secondary components of HD 176318 and HD 194495. If each of these secondaries is about three magnitudes fainter than its respective primary, any spectrogram, no matter how it is made, will register predominantly the light of the primary star. We agree that observations in a different spectral region are desirable, especially, perhaps, in the red and infrared regions where the light of a normal secondary component would be relatively stronger.

Gibbons and Hawking find an apparent secondary maximum in the frequency distribution of e for double-line binaries that seems to us interesting. In view of the selection effects discussed above, this secondary maximum must correspond to a real effect in the velocity curves, provided that it is statistically significant, which, of course, is doubtful in so small a sample. Because seven of the eight systems that form this maximum contain stars of early B spectral types (for which the concentration of circular orbits should be greater because Δ and Δ' are large for stars of this type) the most likely explanation appears to us to be that these velocity curves are distorted in a way analogous to that in which velocity curves of Algol-type systems are distorted.

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Drs Hawking and Gibbons write: The two main points that Batten and Olowin make about our paper are:

1. The measured eccentricities of short period binaries are unreliable and may not represent real eccentricities.
2. There may be a selection effect which makes the detection of higher eccentricities more likely in single-line binaries than in double-line binaries.

We must agree with the first point. Since our letter was published there has appeared a recomputation of 201 G Sgr (HD 184035), which was one of the single-line binaries which we suggested might contain a black hole in view of its reported eccentricity of 0.09. The new computation of Lucy and Sweeney[1], however, lowers this value to 0.049. If this is correct it seriously weakens our argument, because it reduces the number of single-line binaries in our sample with "high" eccentricities from 3 to 2 whereas one would expect 1 on average, if the distribution of eccentricities for single-line binaries were the same as that for double-line binaries (but see Gott[2], succeeding communication).

Although measured eccentricities may be rather unreliable, we do not see any obvious reason why these should favour single line rather than double-line binaries. The selection effect mentioned by Batten and Olowin would appear to us to be small—indeed they admit as much when they say "its total effect in a large sample should not be large". Surely a selection effect which has a small effect in a large sample will have a small effect in any sample. The possibility of statistical fluctuations in a small sample is a separate problem.

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Further Evidence for Collapsed Objects in Binary Star Systems

IT would be of great interest to discover a collapsed object (neutron star or black hole) as one component of a binary star system. Trimble and Thorne[1] have compiled a list of fifty candidate systems from Batten's[2] catalogue. These are non-eclipsing single-line spectroscopic binaries in which the unseen companion has a mass estimated to be greater than $1.4\ M_{\odot}$. These unseen companions are thus too massive to be non-rotating white dwarfs (although the possibility that they are rapidly, differentially rotating white dwarfs cannot be completely excluded as Ostriker and Bodenheimer[3] have shown). In principle, some of these unseen companions could be neutron stars or black holes. In most cases, including all those to be considered here, the unseen companion is less massive than the observed primary star and can be a normal main-sequence star, which is not observed simply because it is considerably less luminous than the primary. Recently, however, Gibbons and Hawking[4] have presented evidence that suggests that one or more of the systems on the Trimble and Thorne list contain collapsed objects. Their argument is as follows. Let the initial binary system consist of two stars with masses M_1 and M_2. Let the more evolved star (M_1) eject some of its mass and collapse to form a neutron star or black hole with gravitational mass M_{N1}. The ejected mass-energy can be in the form of a shell of matter or gravitational radiation, for example. If the initial orbit is circular and the mass loss can be treated as instantaneous and spherically symmetric, then the resultant binary system (M_2, M_{N1}) will have an orbital eccentricity given by

$$e = \frac{M_1 - M_{N1}}{M_2 + M_{N1}} \qquad (1)$$

(Note: the notation for the star masses above is not the usual notation for spectroscopic binaries.) Three of the seven systems from the Trimble and Thorne list with $P < 5$ days were found to have $e > 0.08$. By a comparison with short-period double-line binaries Gibbons and Hawking concluded that the probability of this occurring by chance is only 8%. This suggests that in one or more of the three systems, the eccentricity arises from a sudden mass loss and that the unseen companion is a collapsed object rather than a main-sequence star.

Table 1 Single-line Binaries from the Trimble and Thorne List with $P<5$ Days, $e<0.13$

Star	Spectral type	Aprox-imate distance	Period (days)	e	Corrected radial velocity V_R (km s^{-1})	$\frac{\lvert V_R \rvert}{\langle V_r^2 \rangle^{\frac{1}{2}}}$
HD 40005	B3V	430 pc	3.306	(0.037)	+5	0.5
201 G Sgr	A3III	140 pc	4.625	(0.049)	+18	1.2
HD 191473	B0.5V	1,500 pc	4.2876	0.070	+2	0.2
HD 198784	B3	440 pc	3.30353	(0.024)	+10	1.1
HD 209961	B2V	460 pc	2.1721	(0.0)	−3	0.3

These results must be revised somewhat in light of the recent work by Lucy and Sweeney[5] which indicates that the originally quoted value of $e = 0.9$ for 201 G Sgr was entirely the result of observational error. Tables 1 and 2 tabulate the relevant data for the 7 binaries with $P < 5$ days from the Trimble and Thorne list. Eccentricity data are taken from Lucy and Sweeney whenever possible. A value in parentheses indicates that a circular orbit is compatible with the observational data. We note that the data for HD 176318 and HD 194495 are sufficiently accurate to assure that these are in fact high eccentricity systems. Following the procedure of Gibbons and Hawking, we select for comparison double-line binaries with $P < 5$ days, with both components $> 1.4\ M_{\odot}$, with observational quality a to d in Batten's system, and for which the eccentricity was not assumed to be zero. We likewise exclude

Table 2 Single-line Binaries from the Trimble and Thorne List with $P<5$ days, $e>0.13$

Star	Spectral type	Approximate distance	Period (days)	e	K_1 (km s^{-1})	$\frac{M_2}{M_\odot}$	$\frac{\overline{M}_{N1}}{M_\odot}$	Corrected radial velocity V_R (km s^{-1})	$\frac{\lvert V_R \rvert}{\langle V_r^2\rangle^{\frac{1}{2}}}$	Predicted values	
										$\frac{1}{2}\overline{V}_{sp}$ (km s^{-1})	$\frac{\overline{M}_1}{M_\odot}$
HD 176318	B6V	190 pc	2.912225	0.169	79.3	4.5	2.2	−13	1.4	16	3.3
HD 194495	B7	300 pc	4.9052	0.133	82.2	4.0	2.7	+24	2.4	9.5	3.6

γ Andr B from consideration. Of the 48 double-line binaries satisfying the above criteria only 5 have $e>0.13$. On this basis, the probability that we would find 2 or more out of a sample of 7 with $e>0.13$ is only 16%. Gibbons and Hawking's claim that the Trimble and Thorne list (with $P<5$ days) contains an unusual number of high eccentricity systems is still quite valid.

We present here a test of the hypothesis of Gibbons and Hawking based on the fact that a high eccentricity is not the only consequence of a sudden mass loss. I have shown[6] that a sudden mass loss from M_1 imparts a velocity V_{sp} to the resultant binary system (M_2, M_{N1}) and that V_{sp} is given by

$$V_{sp} = e \frac{M_2}{M_{N1}} \frac{K_1}{\sin i} \tag{2}$$

where K_1 is the observed radial velocity semi-amplitude of the star M_2 and i is the inclination of the orbit with respect to the line of sight. The resultant system (M_2, M_{N1}) is left with this additional velocity because its momentum must balance the net momentum carried away by the ejected matter. If mass loss is indeed responsible for the high eccentricities of the two systems in question we would expect these systems to show higher than average velocities as well. Because they are all spectroscopic binaries for which velocity curves have been obtained, the mean radial velocities of all the systems have been accurately determined. The distance to each binary was estimated by comparing the observed visual magnitude with absolute magnitudes as a function of spectral type as given by Cox and Guili[7]. An absorption coefficient of 1.0 mag kpc^{-1} was used and stars were assumed to be on the main-sequence if no luminosity class was known. The observed mean radial velocities could then be corrected for differential galactic rotation as well as for the solar motion. The corrected radial velocities (V_R) are displayed in the tables and are compared with the r.m.s. corrected radial velocity ($\langle V_r^2\rangle^{\frac{1}{2}}$) expected for a star of corresponding spectral type and position in the sky. For systems with spectral types B0–B5, the velocity ellipsoid for B0 stars is used to compute $\langle V_r^2\rangle^{\frac{1}{2}}$ while for systems with spectral types B6–A3 the velocity ellipsoid for A0 stars was used. The velocity ellipsoid data were taken from Delhaye[8]. Since HD 40005 is a member of the I Orion Association, V_R for this system is taken to be its radial velocity with respect to the stars in the Trapezium. The distribution of $V_R/\langle V_r^2\rangle^{\frac{1}{2}}$ for a random sample of stars is gaussian with a standard deviation of 1.0. The probability that a random sample of 5 stars would produce a larger value of $\chi^2=\Sigma\ V_R^2/\langle V_r^2\rangle$ than that shown by the 5 binaries in Table 1 is 70%. Thus, these binaries possess lower than average velocities. By contrast, the two high eccentricity systems ($e>0.13$) show abnormally high velocities as a group. The probability that a random sample of two stars would produce a larger value of $\chi^2=\Sigma\ V_R^2/\langle V_r^2\rangle$ than that shown by the two binaries in Table 2 is only 2%. For the three systems, $\frac{1}{2}\overline{V}_{sp}$, the median value of the radial component of the imparted velocity due to mass loss is computed from equation (2). The mass of the observed star (M_2) is estimated from its spectral type and the mass of the unseen companion (M_{N1}) is estimated from the observed mass function $f(M)=M_{N1}{}^3\sin^3 i/(M_{N1}+M_2)^2$. Throughout we take $\sin i=\sqrt{3}/2$ (its median value). The values of $\frac{1}{2}\overline{V}_{sp}$, M_2 and $\overline{M}_{N1}$ as well as $\overline{M}_1$, the mass of the evolved star just prior to mass ejection, are tabulated for each system in Table 2. It is clear that the predicted values of $\frac{1}{2}\overline{V}_{sp}$ are of the right order of magnitude to explain the large radial velocities found for the two systems. The fact that the two high eccentricity systems show abnormally high velocities as a group and that these can be explained by the sample mass loss theory strongly supports the tentative conclusion of Gibbons and Hawking that one or more of these systems has suffered mass loss and that the unseen companion is not a normal main-sequence star.

For both HD 176318 and HD 194495 the mass of the more evolved star ($\overline{M}_1$) is found to be less than the mass of the less evolved star (M_2). This is a situation we could expect to find in such close binary systems. M_1 begins as the more massive star and evolves more rapidly. As it becomes a red giant it expands beyond its Roche lobe and begins to deposit matter on the star M_2. Eventually M_1 is expected to become the less massive of two stars. This mass exchange process in close binaries is discussed in detail by Plavec[9]. In some cases such a process can leave the star M_2 with observable abundance anomalies. If abundance anomalies traceable to mass exchange can be found in the spectra of HD 176318 or HD 194495 it would constitute strong additional evidence that the unseen companion is the more evolved star and thereby likely to be a neutron star or a black hole.

The unseen companion in HD 194495 is estimated to have a mass greater than 2.2 $M_\odot$ ($\sin i=1.0$). This is greater than the upper mass limit of 1.95 $M_\odot$ found for non-rotating neutron stars by Hartle and Thorne[10]. The mass of the unseen companion in HD 176318 may be either above or below this limit depending on the value of sin i. A separate study of single line binaries[6] has revealed another promising candidate, HD 59543, which is not discussed here.

To summarize, there are an unusual number of high eccentricity systems on the Trimble and Thorne list (with $P<5$ days). In the present study I find a strong correlation between high velocities and high eccentricities. This evidence supports the suggestion that one or both of the high eccentricity systems may harbour a neutron star or a black hole. These two systems merit further investigation.

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Past Wind Strength from Isotope Studies

IN this communication we explore the possibility that isotope studies can give palaeoclimatological data in addition to the well known determinations of past temperatures[1-3]. We consider that the temperature difference between the equatorial and polar regions (ΔT) largely determines the storminess of our weather, and we will show that this information is recorded in the $^{18}O/^{16}O$ and $^{2}H/^{1}H$ ratios of the ice in the Greenland and Antarctic ice caps.

As a parcel of air moves from low latitudes to progressively colder regions, the water which is precipitated in the form of rain or snow is enriched in ^{18}O (and ^{2}H) with respect to the remaining vapour[4,5]. Thus the vapour in the parcel of air becomes steadily enriched in ^{16}O and ^{1}H as it moves to colder regions, and from the $^{18}O/^{16}O$ ratio of the precipitation at a particular point the temperature difference between that point and the equatorial region (Δt) can be calculated. Exactly equivalent data are obtained from $^{18}O/^{16}O$ and from $^{2}H/^{1}H$ studies, so for simplicity only $^{18}O/^{16}O$ work is considered here.

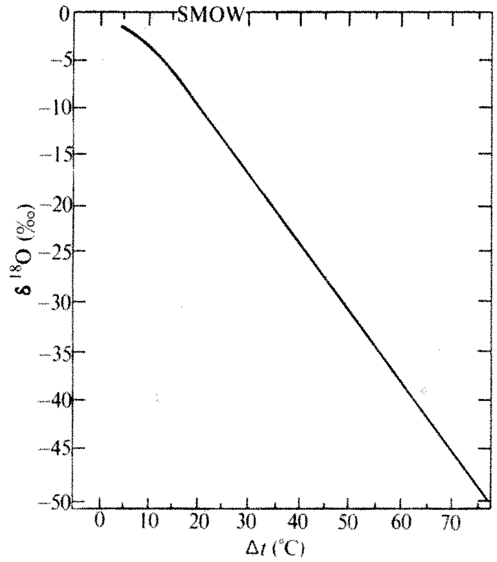

Fig. 1 Plot of temperature difference between the equatorial regions (25° C) and various points on the Earth versus depletion in ^{18}O of the precipitation measured in parts per thousand with respect to standard mean ocean water (SMOW). Data from Dansgard[5].

Using published data on the isotopic composition of present-day precipitation[5], a plot of depletion of ^{18}O in precipitation at a given point against the temperature difference between that point and equatorial regions (Δt) can be prepared (Fig. 1). The study of Δt as a function of time for various regions of the Earth, using data from speleothems or water stored since glacial times in aquifers is an interesting problem in itself, but to obtain a measure of the past storminess of the Earth's weather requires the determination of (ΔT), the temperature difference between equatorial and polar regions. This information is now available in the form of $^{18}O/^{16}O$ profiles through the Greenland ice sheet at Camp Century (77° N)[6], and $^{18}O/^{16}O$ and $^{2}H/^{1}H$ profiles through the Antarctic ice sheet at Byrd Station (80° S)[7,8]. These data are presented in Figs. 2 and 3 as plots of the depletion of ^{18}O (with respect to standard mean ocean water, SMOW) in the precipitation versus time for Greenland and Antarctica. From Fig. 1 the data can be read as a plot of the variation of ΔT over the past 100,000 yr for both hemispheres. The most striking result is that during glacial periods the temperature difference between the equatorial and polar regions increased by 20 to 25%—in other words, glacial periods seem to be characterized by increased vigour of the wind circulation.

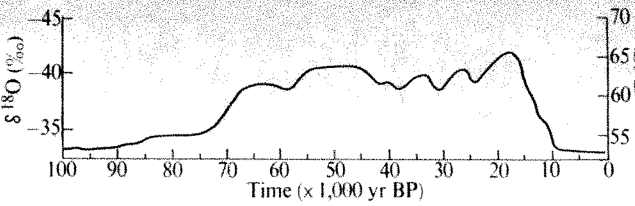

Fig. 2 Temperature difference between south polar region and tropics during past 100,000 yr. Data from Dansgard[5] and Epstein *et al.*[7,8].

Strictly speaking, various corrections should be applied to the curves as follows: First, because neither ice core came from the centres of the respective ice sheets, the deeper parts of the cores contained snow which fell progressively further inland, with perhaps slightly different climatic conditions. From Figs. 2 and 3, however, we may see that the value of ΔT in the last interglacial is similar to that in the present interglacial, and, because this is a comparison between the top and the bottom of the core, any correction must be small. Second, the isotopic composition of the ocean changed due to the removal of water depleted in ^{18}O from the oceans to form the great ice sheets of the northern hemisphere during the Glacial Period. This is a very small effect, changing the world's oceans by no more than 1 to 2 parts per thousand, and would lead to an underestimate of the increase in ΔT during the Glacial Period. Third, the thickness of the ice sheets may change between glacial and interglacial periods. Briefly, because both the Greenland and Antarctic Ice Sheets are bounded by the sea, both now and in glacial times, the biggest effect is caused by the lowering of sea level which increases the area of the ice sheet[9]. This greatly increases the thickness on the margins of the ice sheet but has only a small effect in the central part of the sheet.

The isotopic data from the Greenland and Antarctic cores suggests that when the Earth cools, ΔT increases, that is, the polar regions cool more than the tropics. This is probably because cooling causes greater albedo changes at high latitude, attributable to increased ice and snow cover, and hence reduces the solar energy input. This might explain why the increase in ΔT for the northern hemisphere during the last glacial period was greater—25% (Fig. 3)—than for the southern hemisphere—20% (Fig. 4)—where most of the high latitude land is snow and ice covered even in interglacial times. On this model even the present weather would be a result of the fact that our polar regions have an increased albedo because of snow and ice cover. If the melting point of water were, say, 5° lower, our weather would be much more benign.

Fig. 4 is a generalized plot of how ΔT changes with temperature of the equatorial regions. An implication of this curve is that if the Earth were to warm, ΔT would decrease, that is,

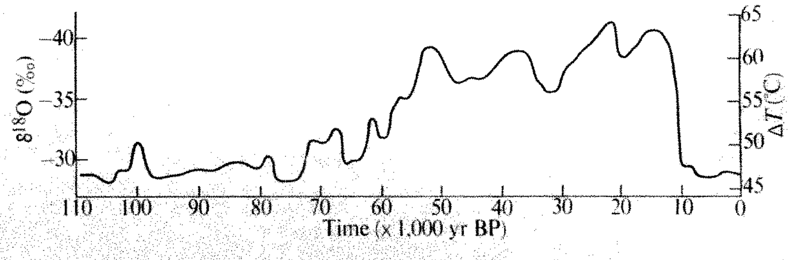

Fig. 3 Temperature difference between north polar region and tropics during past 100,000 yr. Data from Dansgard[5] and Dansgard *et al.*[6].

the polar regions would be warmed more than the tropics. This suggests that warmer periods in the past—say early Tertiary times—were periods of less wind and where the equator was only slightly warmer but the regions of higher latitude were much warmer. There is considerable plant fossil evidence to support at least the latter of these conclusions (see, for example, refs. 10 and 11).

If the glacial periods are in fact periods of much more violent weather, this should be recorded in the geological record. Glacial periods are normally associated with the formation of ventifacts and extensive loess deposits, derived from material supplied by glacial flood plains. Others, including the classic loess deposits in China, were far removed from any ice sheet and can probably only be explained in terms of greater windiness in the China/Gobi Desert area. Similar arguments can be advanced for the fossil sand dunes of central Australia. Australia was far removed from any ice sheet and is believed to have been wetter during the last glacial period. Yet large dune systems now dormant were probably active at that time. The only possible explanation seems to be that the glacial period in Central Australia was a period of significantly greater windiness than at present. In North America there is considerable evidence for greater windiness during the most recent and earlier glacial periods. For example, in the Sweetwater and North Platte drainage systems there was considerable deflation and dune formation during the last glacial period, whereas in post-glacial times the dunes have been stabilized and there is little wind erosion (G. Richmond, personal communication). Again, in central and western Nebraska dunes which were moving in glacial times are now stabilized[12].

As well as the very large temperature fluctuations (6° C) between glacial and interglacial periods, the Earth goes through small temperature fluctuations (1.5°–2° C) (see, for example, Lamb[13]). There was a very warm period in the twelfth and thirteenth centuries (so-called "Little Climatic Optimum") with a sharp decrease in the fourteenth century into the so-called "Little Ice Age" of the fifteenth, sixteenth, seventeenth, eighteenth and early nineteenth centuries. The Antarctic core has not been measured with sufficient detail, but the Greenland curve shows that even these smaller temperature fluctuations have increased ΔT. Fig. 5 has been calculated from Dansgard's data[6] and shows that the transition from the Little Climatic Optimum to the Little Ice Age involved an increase in ΔT of 1° C or about 2.5% with a consequent increase in storminess.

This sharp change in climate may have important implications in meteorology and history. For example, it may have been the increase in storminess that led the Vikings to abandon their North Atlantic route with the onset of a cold period rather than seek a more southern route. Similarly, the Polynesian migrations in the Pacific started with the onset of a warm period and ended at the onset of the Little Ice Age. It has always been difficult to understand how the Polynesians could have settled New Zealand from Tahiti by the early fourteenth century and then not have gone on to discover Tasmania and Australia. If the Little Climatic Optimum had been a period when very violent storms were rare, this would explain how the Polynesians could explore and settle the South Pacific in a few hundred years. If the break in climate in the eighteenth century caused a sharp increase in the frequency of violent storms, the loss of a relatively few skilled navigators could have effectively discouraged further exploration.

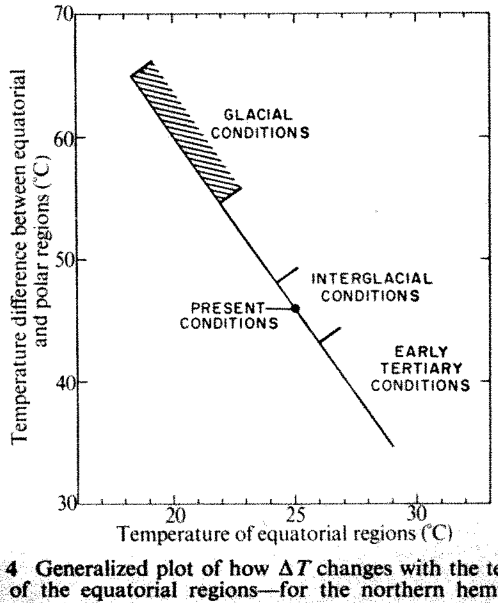

Fig. 4 Generalized plot of how ΔT changes with the temperature of the equatorial regions—for the northern hemisphere.

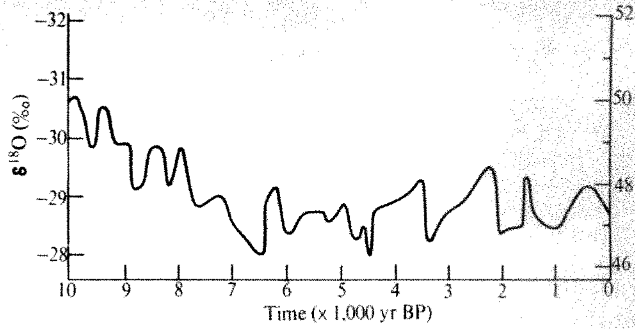

Fig. 5 Temperature difference between north polar region and tropics during past 10,000 years. Data from Dansgard[5] and Dansgard *et al.*[6].

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Imaging the Rhodium Atom with a Conventional High Resolution Electron Microscope

The ability of microscopes to make single atoms of metals visible has been reported by Muller[1] and more recently by Crewe *et al.*[2]. Muller has been working with the direct imaging method of field-ion microscopy, which produces images of single atoms in the surface of solid specimens. Crewe used a high resolution scanning microscope developed in his laboratory to image thorium and uranium atoms in an organic molecule. In neither case was a conventional electron microscope used.

Although resolutions of better than 0.2 nm (2 Å) have been reported with conventional transmission electron microscopes, little hope had been given that these instruments could be used to obtain the image of a single atom. The problem was one of lack of contrast between the heavy atoms and their support. Crewe overcame this contrast problem by using a special electron detector placed in a position which discriminated between the elastic and inelastic scattered electrons and measured primarily the elastically scattered electrons. In our investigation, we have been able to maximize the difference in the elastic scattering of electrons by light and heavy atoms through proper objective aperturing of a conventional transmission electron microscope and have observed for the first time individual rhodium atoms on silica.

Lenz[3], in his study of the angular intensity distribution of electrons of intermediate energies (50–150 keV) scattered at very small angles, has shown that elastic scattering involves much larger scattering angles than does that for inelastic scattering. The angles of scattering resulting from the elastic scattering process are sufficiently large ($>10^{-3}$ radians) that they can be apertured out in the objective lens of an electron microscope, thereby improving contrast. This is the common practice. Lenz also calculated the ratio of the total elastic scattering cross section, σ_e/σ_i, for atoms of different atomic number. These data can be reduced to the empirical expression

$$\sigma_e/\sigma_i \sim Z/19\text{–}20$$

and is independent of the accelerating voltage of the electron beam. Our objective was to calculate, using Lenz data, the size aperture which, when used in the objective lens of our microscope, would minimize the removal of scattered electrons (inelastic) due to silica from the electron beam while maximizing the removal of electrons elastically scattered by the rhodium. For our microscope, a Philips EM-300 with high resolution objective pole pieces, this condition exists at 5×10^{-3} radians. For the position of the objective aperture in the EM-300, this angle corresponds to an aperture diameter of 30 µm. This size objective aperture was used for our studies of rhodium on silica.

Rhodium catalysts were prepared by impregnating a silica support with an aqueous solution of $RhCl_3:3H_2O$. The silica was 'Cabosil HS5' obtained from the Cabot Corp., Boston. The samples were reduced *in situ* in flowing hydrogen for 16 h at 400° C, the Rh concentration being 1.0 weight %. The degree of dispersion (or surface area) of the Rh after reduction was obtained by measurements of H_2 and CO chemisorption at room temperature. It was found that the Rh was very highly dispersed, with an average crystallite size of 1.2 nm (12 Å). Indeed, the Rh was atomically dispersed in the sense that every Rh atom in the sample was accessible to gas and either adsorbed one hydrogen atom or one CO molecule. The value of 12 Å was later confirmed by direct measurement using the electron microscope. Complete details of catalyst preparation and chemisorption are presented elsewhere[4].

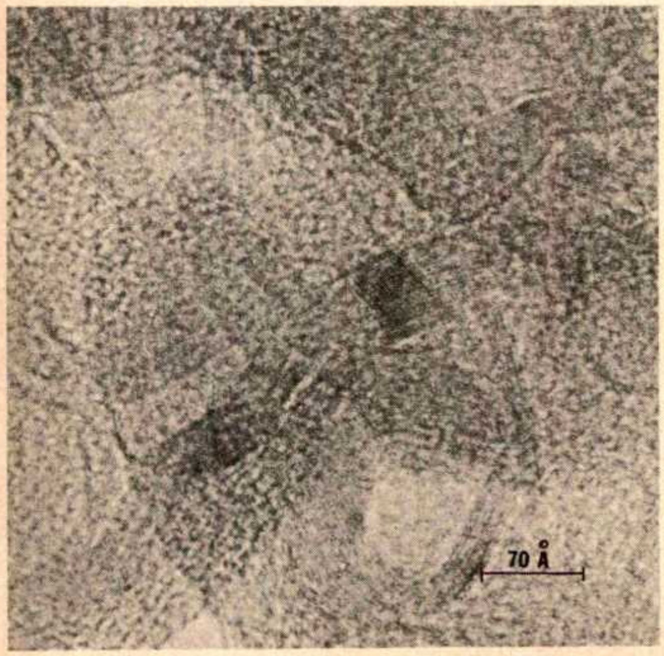

Fig. 1 Graphitized ISAF carbon black used as calibration specimen, d_{002}–0.344 nm. A 30 µm aperture is in place in the objective lens.

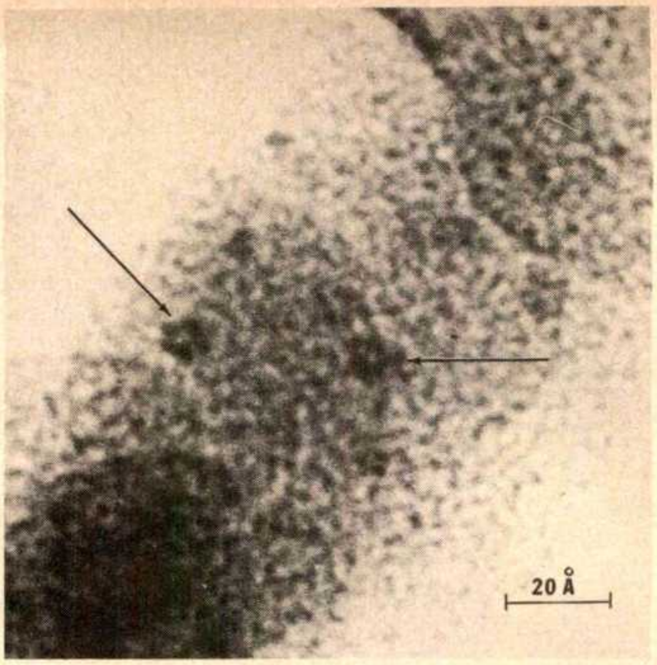

Fig. 2 Rhodium atoms on silica. Arrows indicate clusters of rhodium atoms. A 30 µm aperture is in place in the objective lens.

No modifications of the electron microscope were made, other than using a pointed filament (Ladd Research Industries) to provide a more coherent electron beam. The laboratory housing the microscope, however, has been specially constructed to reduce vibration to less than 2×10^{-6} inches s^{-1} and is shielded from stray magnetic fields. The area surrounding the specimen was cooled to −160° C to reduce contamination (<0.1 Å min^{-1}) and changes of astigmatism during operation of the microscope.

The catalyst sample was ground and ultrasonically dispersed in butyl alcohol with a small amount of partially graphitized ISAF carbon black and deposited on a "holey" carbon film. The ISAF carbon black was used as an internal magnification and resolution standard as suggested by others[5]. The micrograph of the black shown in Fig. 1 was taken with the 30 µm objective aperture in place. This shows the 0.344 nm (3.44 Å) 002 spacing and attests to image quality in the molecular size range. Contrast is lower than that obtained on the carbon black when the aperture is not used but is sufficient to allow instrument checks under exactly the same conditions as those used on the catalyst.

Fig. 2 is a micrograph of rhodium on silica using a 30 µm objective aperture. Clusters are visible that are probably rhodium atoms and are approximately 1 nm (10 Å) in diameter with the diameter of the individual spots in the cluster being 0.27 nm (2.7 Å) ± 0.02 nm. This value corresponds closely to the atomic diameter of rhodium given by Hume-Rothery and Raynor[6] of 0.2690 nm. The spacings between the atoms measured from the micrograph are 0.35–0.40 nm. Again, this is in good agreement with the lattice spacing given for the face-centred cubic structure given for rhodium of 0.3805 nm. Resolution of the clusters into individual atoms was obtained on successive micrographs of the same field and at ±3° tilt of the specimen about the axis of the electron beam.

We feel that these data, and micrographs obtained from other heavy metals, indicate that we have succeeded in obtaining images of isolated individual atoms using a conventional high resolution electron microscope. Data of this type can be of considerable help in obtaining the detailed structure of supported metal catalysts in respect to the clustering of the metal and the topographic details.

Note added in proof. The referee has pointed out to us that the principle of optimal sizing of the objective aperture for differential contrast had been previously suggested in a theoretical study by Cosslett (*Lab. Invest.*, **14**, 1009; 1965); we were not aware of this work when our calculations were made.

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Silver 108*m* Dating in Marine Organisms

WE have read with interest the recent letter by Beasley and Held[1] which voices reservations concerning the origins of the ^{108m}Ag and ^{110m}Ag reported by us[2]. Their comments are well thought out and deserve a careful reply.

First, we did not mean to imply that the ^{108m}Ag and ^{110m}Ag observed in the Pacific marine organisms was actually produced primarily by thermal neutron activation of stable silver; only that the assumption of an initial ^{110m}Ag/^{108m}Ag activity ratio value of 162 yielded apparently reasonable dates of original production of the radiosilver falling within the 1961–1962 atmospheric nuclear weapons testing period. It is true that the value 162 came from a reactor experiment[3] involving thermal and epithermal neutrons. But we first assumed it, not for this reason, but rather because it was then the only number available to us. We continued to use it because, rather remarkably, it gave reasonable results.

As Beasley and Held suggested, the reaction ^{109}Ag(n,2n) ^{108m}Ag does seem to be important in thermonuclear bomb production of radiosilver. More recent measurements, which we have just concluded on a sizable number of marine organisms collected in 1964–1965, suggest that the radiosilver in those samples had a rather uniform initial ^{110m}Ag/^{108m}Ag activity ratio of about 180. We consider this last value to be the result of a combination of fast neutron capture on ^{109}Ag and on ^{107}Ag, which should produce an initial ratio of about 400, together with ^{108m}Ag production by the ^{109}Ag(n,2n) reaction.

Beasley and Held also cited measurements in the environment of radiosilver from pre-1959 nuclear weapons testing, and suggest that ^{108m}Ag left over from that period might be expected to affect the radioactive datings made by us on 1964–1965 marine biological samples. We have found one sample collected directly downstream from the US Pacific Proving Ground in 1964 which does seem to contain some pre-1959 ^{108m}Ag. In general, however, we believe that radiosilver from the latter period should have an insignificant effect on the ^{110m}Ag/^{108m}Ag datings of 1964–1965 samples, based on (1) the fact that many more megatons of thermonuclear weapons were reported[4] detonated in the atmosphere in 1961–1962 than pre-1959, (2) the effects of turnover in the environment between the two periods and (3) the nature of the dating formula.

Beasley and Held state in their letter that the (n,p) reactions on stable cadmium are probably not important as producers of ^{108m}Ag and ^{110m}Ag in thermonuclear explosions "because the quantity of stable cadmium in nuclear devices would probably be kept to a minimum on account of the large thermal neutron cross sections". But it has been reported[5] that there was one shot in the 1962 US Test Series into which cadmium was intentionally introduced to produce a tracer of ^{109}Cd, namely the "Starfish Prime" explosion of July 9, 1962, at an altitude of about 400 km over Johnston Island. The possible presence of 1964–1965 environmental samples of radiosilver from cadmium in this explosion must also be considered, as it is not immediately obvious that such production would have been insignificant in comparison with other production during the 1961–1962 testing period.

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BIOLOGICAL SCIENCES

Chromosome Analysis of Abnormal Cells

I REGRET to say there was an error in my recent communication "Chromosome Analysis of Abnormal Cells"[1]. In Fig. 2 cell *a* is shown with only fifty-four chromosomes whereas cell *b* has

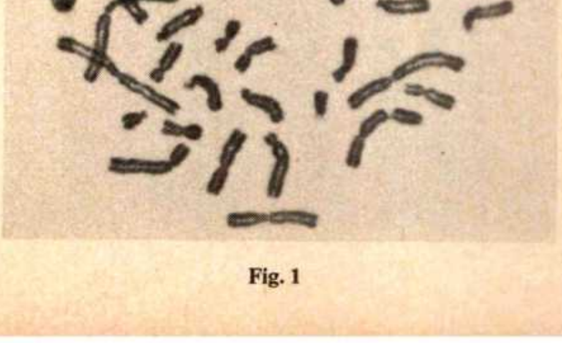

Fig. 1

fifty-five chromosomes. In preparing Fig. 2*a* one chromosome was unfortunately omitted although it was included in Fig. 3, the correct interpretation of the two cells. The chromosome in question is ringed on Fig. 1 here and would have been placed in group *G* of the Denver–London system.

Although this error is most regrettable, it does not in any way alter or invalidate the argument put forward in my letter concerning the unsuitability of the Denver–London system for analysing highly abnormal chromosome constitutions.

I thank Professor P. C. Koller for bringing this mistake to my attention.

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Variant of the Fluorescence Pattern in an Abnormal Human *Y* Chromosome

WILSON *et al.*[1] and Morillo-Cucci and German[2] have reported on large *Y* chromosomes with a terminal non-fluorescent segment of the long arms. We have found another variant of the fluorescence pattern in a large *Y*.

Our subject was a 36 yr old healthy man of normal body proportions, whose chromosomes were analysed because his first child, a female, had died with the clinical diagnosis of the trisomy 13 syndrome. His son, who is 4 yr old now and clinically healthy, has the same variant *Y* chromosome as the father: the *Y* chromosome was consistently as large as the *D* group chromosomes. No prominent constriction was seen in orcein-stained preparations, although some fuzziness could be demonstrated along the whole length of the long arms, as described for normal *Y* chromosomes. Quinacrine dihydrochloride fluorescence staining of blood cultures showed a non-fluorescing gap at about the midpoint of the strongly fluorescing portion of the long *Y* arm. This gap was consistently found in all metaphases examined (Fig. 1). The consistency of this finding in all metaphases regardless of chromosome contraction differentiates this constriction from the occasionally occurring less fluorescing gap of normal-sized *Y*s.

The explanations put forward by Wilson and coworkers[1] also apply to our cases. Either the fluorescence patterns of long *Y* chromosomes show variants of different kinds, or this case and other cases of abnormal *Y* chromosomes represent examples of structural rearrangement. Morillo-Cucci and German[2] assumed a duplication of a portion of the long *Y* arm in their case. In our case a duplication of *Y* long arm material including a small part of the non-fluorescing portion, or, less probably, an insertion of autosomal or *X* chromosome material into the intensely fluorescing part of the long *Y* chromosome, would be possible explanations.

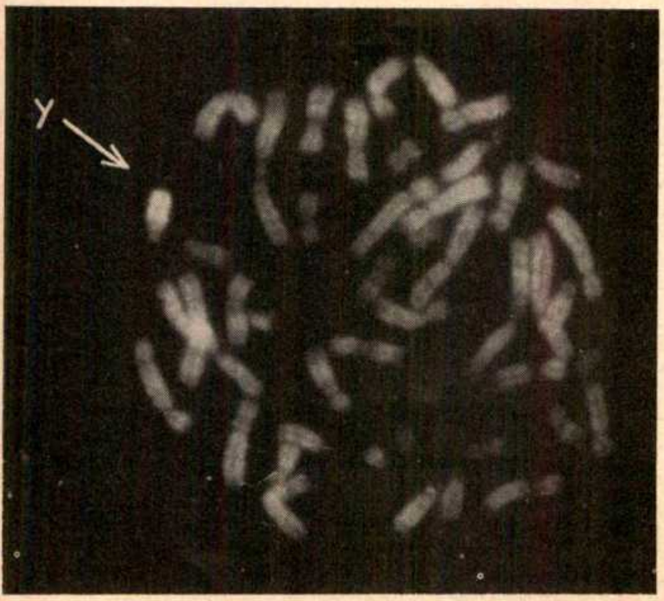

Fig. 1 Chromosomes showing the abnormal *Y* with a non-fluorescing gap.

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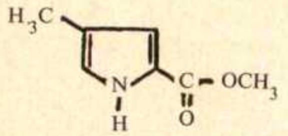
Identification of the Trail Pheromone of a Leaf-cutting Ant, *Atta texana*

THERE are numerous reports of the isolation and identification of insect sex pheromones, and recently a termite trail-following pheromone was isolated and identified[1], but this is the first isolation and identification of an ant trail pheromone to be reported. We have identified the major volatile component of the trail marking substance laid down by the town ant, *Atta texana* (Buckley), as methyl 4-methylpyrrole-2-carboxylate (I). The worker ants of *Atta texana*, whose trail marking substance contains both volatile and nonvolatile components[2], readily followed trails made by us with synthesized (I).



(I)

The whole bodies of 3.7 kg of worker ants of mixed sizes obtained from Grant Parish, Louisiana, were macerated in methylene chloride and the soluble material was distilled in a short-path still onto a condenser (cooled with dry ice) at 90° C and 0.05 mm Hg. The trail-following response[3] of the minor workers from a laboratory colony was used to monitor this and all subsequent isolation steps. The active nonvolatile material was saved for future study, and the volatiles were used for this investigation. The active distillate was fractionated by gas chromatography. Successive vapour phase chromatography (VPC) of the major active component on four columns (SE-30, diethylene glycol succinate, Carbowax 20 M, and silicone DC QF-1) yielded 150 μg of a single compound. This very potent trail pheromone, when rechromatographed on the columns, gave a single symmetric peak on each column. Four other VPC fractions, which have not been purified or identified, are active at about ten times higher concentrations than the major active compound and are present in about five to twenty times smaller amounts.

On the basis of mass, infrared, and nuclear magnetic resonance spectra, we assigned structure (I) to the pheromone, which was confirmed by congruence of these data and of VPC retention times with those properties of an authentic synthetic sample[4].

Potency of the synthesized (I) was evaluated by describing on slick cardboard sheets, 50 cm circumference circles with serially diluted 10 μl. chloroform solutions. Twelve minor workers from a laboratory colony were then released into the centre of the circle. The lower threshold of detection was 0.08 pg/cm (3.48×10^8 molecules/cm), about the same as that recorded for *R. virginicus*[1]. Thus only 0.33 mg would be required to draw a detectable trail around the world. Strong responses were obtained from 0.8, 8.0, and 80.0 pg/cm, but 0.8 ng/cm produced some repellency. Minor workers were completely repelled by concentrations of 8.0 ng/cm and above. Volatility of the pheromone was demonstrated by placing the minor workers on plastic sheets 1 mm above the trail[2]. Workers detected the odour at a concentration of 80 pg/cm and strongly responded at 0.8 ng/cm described on the trail below the plastic sheet.

Medium and large workers were then tested on natural trails leading from nests in the field. They readily followed a 2.7 pg/cm trail on a 15 cm strip of cardboard placed across an "erased" portion of the trail. They detected another trail made by dribbling 4.0 pg/μl. on the sand at a 45° angle to the field trail; response was strong at 40.0 pg/μl.

We thank Dr Henry Rapoport for 4-methylpyrrole-2-carboxylic acid. This work was supported by a US Public Health Service grant.

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Design and Synthesis of Controlled Release Pesticide-Polymer Combinations

ALTHOUGH the indiscriminate dissemination of pesticides into terrestrial and aquatic ecosystems is reprehensible, the magnitude of the pest control problem will necessitate the use of these materials for the foreseeable future. Persistent pesticides are undesirable because of their frequent incorporation into the food chain[1-3]. On the other hand, pesticides with short lives tend to be ineffective. In both cases, the amounts applied are often grossly in excess of that actually required to control the pest because of the need to compensate for pesticide loss by leaching and evaporation. We have therefore investigated the potential of pesticide-polymer combinations as a means of securing controlled release of a biodegradable pesticide in approximately the correct amount needed over an appropriate period of time.

The fundamentals of such controlled release systems are currently being investigated primarily for forestry applications such as the 5 yr suppression of competitive deciduous brush in the presence of conifers in the temperate Pacific North-West[4-6] and in tropical Costa Rica[7], the prevention of damaging attack on commercially valuable mahogany and Spanish cedar by the shoot-borer, *Hypsipyla grandella* Zeller. Two distinct approaches are now reported. (*a*) Pesticide release by diffusion through polymers, and (*b*) pesticide release by degradation of a polymer containing the pesticide as a pendent side chain.

For case (*a*) the active pesticide is dissolved or encapsulated in a polymeric matrix and the combination is placed in the medium where pesticidal activity is desired. Release occurs by diffusion so that no specific structural moiety within the pesticide molecule is necessary. The method therefore has general applicability for the controlled release of a wide variety of biologically active materials. Furthermore, a broad range of polymer matrices are also functional although it has now been found that molten polyamides or other polymers containing backbone amide linkages such as polyurethanes are especially versatile because of their remarkable solvent powers for pesticides in general[5] and the fact that this solvency is maintained after cooling. Solid solutions of pesticide (> 25% w/w) in polyamides (M_n, 2,000–15,000) synthesized from ethylenediamine and the dimer of linoleic acid can be routinely prepared. Using the housefly chemosterilant hexamethylphosphoric triamide (HMPT)[8] as a water-soluble model for a typical systemic organophosphorus pesticide and polyamides (M_n, 15,000) from ethylenediamine and dimerized linoleic acid as the matrices, the release rates were determined for a series of cylindrical pesticide-polymer blocks (diameter 3 cm) by contacting only one circular face with vigorously stirred water (200 ml.). The HMPT released, determined by neutron activation analysis, varies with the square root of the elapsed time (Fig. 1) in accord with diffusion theory[5,9]. The general solvency of amidic polymers coupled with computer evaluation of diffusion coefficients can therefore be used to design a wide range of controlled-release pesticide-polymer combinations the duration of whose effectiveness is adjustable. For case (*b*) the pesticides, exemplified by the herbicidal phenoxyacetic acids (RCOOH), are chemically attached as a pendent substituent to a natural or synthetic water-soluble or insoluble polymer

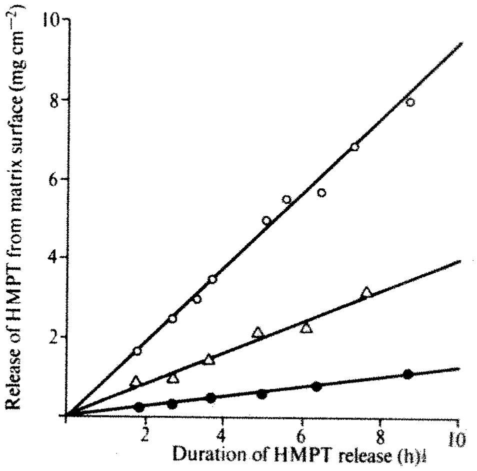

Fig. 1 Rate of release of hexamethylphosphoric triamide (HMPT) from a polyamide matrix. ○, 21.48% HMPT—polyamide solid solution; △, 14.00% HMPT—polyamide solid solution; ●, 6.90% HMPT—polyamide solid solution.

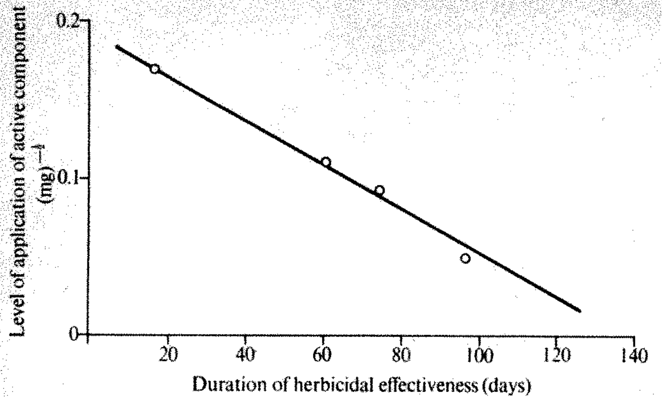

Fig. 2 Relationship of duration of herbicidal effectiveness to level of application for 2-methyl-4-chlorophenoxyacetic acid chemically combined with a water soluble polymer.

having a replaceable hydrogen as formulated in equation (1). Obviously the pesticide must also contain a structural moiety suitable for use as a link to the macromolecule[10], and the carboxyl group is only one of the many alternatives possible.

$$\text{Polymer-X-H} + \text{RCOOH} \underset{\text{environment}}{\overset{\text{synthesis}}{\rightleftharpoons}} \text{Polymer-X-COR} \qquad (1)$$

(X = N, O or S)

Pesticide-polymer combinations of this type can readily be synthesized by, for example, conventional acylation of a solution (dioxan, pyridine) or suspension (benzene) of the backbone polymer using the acid chloride of the pesticide acid[11]. In the biological environment, side chain degradation occurs so that the chemical bonds holding the pesticide within its polymeric prison are sequentially broken to provide a sustained release of the pesticide over an extended period of time. The rate of release will clearly be determined by the nature of the pesticide-polymer bonds, the chemical characteristics of the pesticide and polymer and the dimensions and structure of the resultant macromolecular combination. Where the polymeric backbone is water-soluble the duration of pesticide release (D_{pr}) for n spherical particles (radius r and density ρ) of the pesticide-polymer combination in a water-saturated heterogeneous surface reaction is given by

$$D_{pr} = \rho r_o/k_h C_o - (R_h \rho^2/n\pi k_h^3 C_o^3) \qquad (2)$$

where C_o is the initial concentration of pesticide-polymer linkages on the surface of a particle of radius r_o, R_h is the rate of hydrolytic degradation and k_h is the hydrolysis rate constant. Since each pesticide molecule released by hydrolysis exposes another pesticide-polymer linkage beneath, C_o is a constant and the duration of pesticide release (D_{pr}) can be predicted from equation (3) in which

$$D_{pr} = A - B\sqrt{W} \qquad (3)$$

where A and B are constants and W is the amount of pesticide-polymer combination used. The validity of this equation is demonstrated by the linear plot (Fig. 2) of the persistence of herbicidal activity[5] exhibited by a polymer synthesized by the partial acylation (56.1%) of polyvinyl alcohol with 2-methyl-4-chlorophenoxyacetyl chloride. The duration of pesticide release was determined by observation of the inhibition by a herbicide of seed germination in lettuces sown daily. Equation (3) also defines the minimum amount of pesticide-polymer combination ($W = A^2/B^2$ when $D_{pr} = 0$) necessary for pesticidal activity.

On the other hand, the polymeric backbone selected may be water-insoluble and cellulose and lignin, the macromolecules of wood and bark, are particularly appropriate choices because of their long-established biodegradability and ecological acceptability and because of their abundance as low-cost solid wastes[12]. Marine[13] and proteinaceous[14] solid wastes can also be used as the polymeric backbone. Acylation of these natural hydroxylated polymers[15] with a pesticide acid chloride affords pesticide-polymer combinations which degrade by a heterogeneous surface reaction to provide a sustained release of pesticide.

The duration of effectiveness (D_{pr}) of this type of sustained release pesticide-polymer combination is given by

$$D_{pr} = (1/k_d)(\ln W - \ln R_d/k_d) \qquad (4)$$

where W is again the amount of pesticide-polymer combination used, R_d is the rate of degradation and k_d is the degradation rate constant.

Since k_d and R_d are constants for a given system, equation (4) can be simplified so that

$$D_{pr} = M \log_{10} W - N \qquad (5)$$

where M and N are constants. In this case the minimum amount of pesticide-polymer combination necessary for pesticide activity is $10^{N/M}$ ($D_{pr} = 0$). Experimental confirmation of the usefulness of equation (5) in the design of controlled release pesticide-polymer combinations is again provided by the lettuce seed germination bioassay of the release of herbicide acids[4] from esters of cellulose and lignin (Fig. 3).

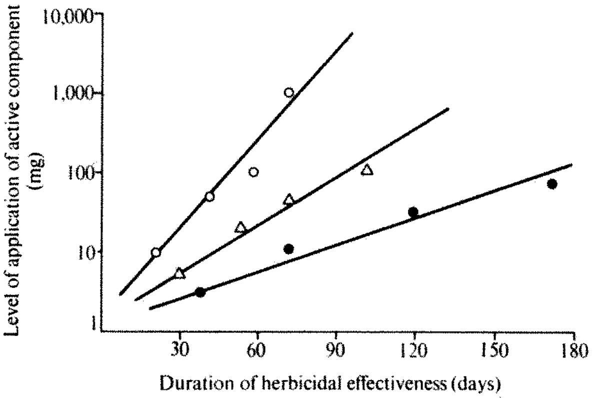

Fig. 3 Relationship of duration of herbicidal effectiveness to level of application for 2,4-dichlorophenoxyacetic acid (2,4-D) chemically combined with water insoluble polymers. ○, 2,4-D alone; △, 19.7% 2,4-D/Douglas fir bark chemical combination; ●, 39% 2,4-D/kraft lignin chemical combination.

The ecological implications of the results in Fig. 3 are particularly profound because the controlled release combinations in comparison with free pesticide provide either an extended period of protection at equivalent levels of application or the same period of protection at greatly reduced levels of application. Clearly, both of these alternatives tend to reduce the environmental hazards associated with the continued conventional use of pesticides. Although developed for forest pest control the systems described should be broadly applicable to the controlled release of other biologically active substances[16].

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Contraction of Single Smooth Muscle Cells from *Bufo marinus* Stomach

MANY aspects of vertebrate smooth muscle function cannot be studied adequately in the whole animal or *in vitro* because the collagen net surrounding individual cells distorts force-time relationships[1]. Electron microscopy of smooth muscle tissues has provided some data on structural changes during contraction[2,3], but the difficulty in obtaining sections in the correct plane and lack of a suitable method for viewing contractile elements in three dimensions has impeded progress. Lowy and Small[4], using a weight to stretch guinea-pig taenia coli during fixation and dehydration, observed a ribbon-like arrangement of myosin filaments but could not study contracted cells prepared the same way.

A method for studying isolated smooth muscle cells would overcome many of the difficulties encountered with smooth muscle as a tissue. A technique for isolating living, beating heart cells using collagenase and trypsin has been developed by Vahouny *et al.*[5], and we have modified it to isolate smooth muscle cells and determine whether they were intact and living.

Bufo marinus circular stomach muscle was used because this animal is relatively cheap, and available throughout the year from suppliers (Lemberger Co., Oshkosh, Wis.), and each specimen can provide a comparatively large amount of circular stomach muscle.

An adult *Bufo marinus* (200–300 g) was double-pithed and the stomach removed and stretched over a glass rod. Fine forceps were used to remove the serosa, and thin strips of the circular muscle were peeled away from the underlying mucosa and pinned to a cork board. Each strip was cut into 2–3 mm segments, and the pieces were placed in a test tube containing 2 ml. of solution A: 0.1% trypsin (Sigma, type III), 0.1% collagenase (Sigma, type I), dissolved in Harris Ringer[6] and maintained at 31° C.

After 1 h of incubation the supernatant was removed and replaced with 1 ml. of solution B which differed from solution A in having only 0.05% collagenase. At 30 min intervals thereafter, the supernatant was removed and replaced with fresh solution B. The supernatant was gently stirred and a small aliquot was placed on a haemocytometer and observed with a phase microscope. It was found that the greatest number of cells were separated after 2.5–3 h of digestion.

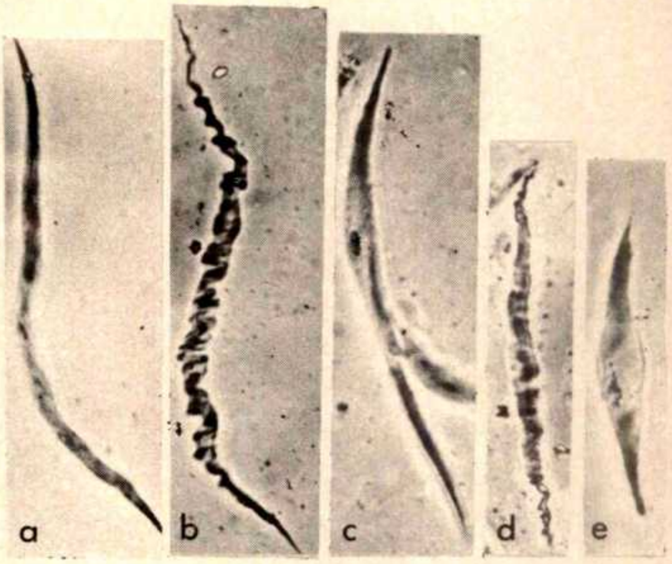

Fig. 1 Examples of cell configurations observed in suspensions of single cells. Phase contrast micrography (×312).

Various configurations were seen among the cells (Fig. 1). Some were long and spindle-shaped (Fig. 1*a*), some were slightly contracted to extremely contracted (Fig. 1*c*, *e*) while others seemed to be coiled or twisted (Fig. 1*b*, *d*). To test for damage to the cells 1% trypan blue in Harris Ringer was mixed with the suspended cells. Lack of staining in 95% of the cells indicated that virtually all cells, regardless of appearance, survived separation[7]. No spontaneous contraction was observed. We tested for contractility by electrical and ionic stimulation.

For electrical stimulation we made a chamber which would produce a sufficient field and which was optically perfect enough for microscopy by cementing cover glasses to a glass slide with epoxy glue so that a shallow trough about 0.15 mm deep and 3–4 mm wide was formed. Two 0.005 inch diameter platinum wires with their ends separated by 3–8 mm were cemented in place with epoxy cement which also served to form the ends of the trough. Silver wires were soldered to the ends of the platinum wires and led to two brass screws fixed to the end of the slide with epoxy glue. Washers and nuts fitted to the screws provided secure, but easily removable, connexion to a Grass S1U5 stimulus isolation unit and S-44 stimulator. The stimulating chamber was mounted on the stage of a Nikon SuKe microscope equipped for photomicrography.

Small samples of supernatant, diluted several times with Harris Ringer to avoid excessive turbidity, were pipetted into the trough, and a cover glass was placed on top. After waiting about 5 min to allow most cells to settle to the bottom, a photomicrograph was taken (Fig. 2*a*). A single stimulus was delivered to the chamber, and after contraction was maximal a second photograph of the same field was taken (Fig. 2*b*). Polarizing filters with fibre axes parallel gave the clearest pictures of cell outlines. The efficiency in achieving contraction in cells depended on duration of stimulus, strength of stimulus and separation of electrodes. With 3 mm separation, a single square-wave pulse of 50 V, 5 ms duration produced maximal contractions in most cells. Not all cells responded to single stimulus, but if a train of 1 ms pulses at 10 Hz was given for 1 to 2 s, virtually all cells contracted. After contraction, cells relaxed slowly, although the cells only occasionally returned to the full length before stimulation. After relaxation, the same cell could be restimulated to contract. We have been able to stimulate a cell to undergo as many as six cycles of contraction and relaxation.

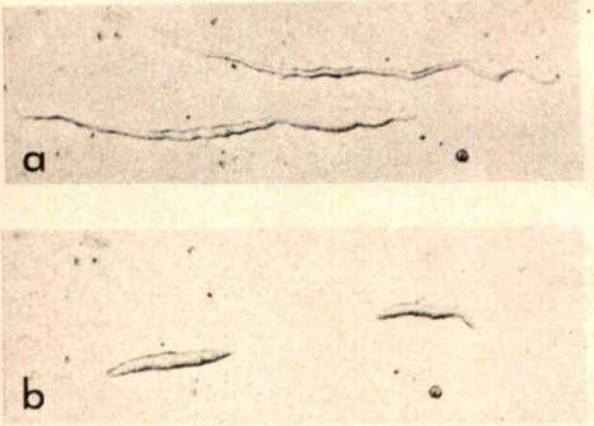

Fig. 2 Micrographs of single cells before (*a*) and after (*b*) a single, square-wave pulse. Note the disappearance of convolutions in contracted cells. Photographed with polarization filters, fibre axes parallel (× 195).

We wondered whether the electrical stimulation was activating the cells through the membrane or whether in cells with damaged membranes the electrical stimulus activated the cells by some non-physiological mechanism. To test for a membrane-mediated response, an equal volume of K Harris Ringer (NaCl and $NaHCO_3$ replaced by equimolar quantities of KCl and $KHCO_3$) was added to the cell suspension in the trough using a 26-gauge needle and syringe while the cells were observed with a Zeiss inverted-body microscope. Although the currents produced by addition of fluid to the trough made it nearly impossible to observe the same cell throughout, once the addition of fluid had stopped the slide could be moved to an area which showed cells still contracting. As with the repetitive stimulation, nearly every cell contracted in response to the K Ringer. We conclude that the cell membrane is intact and capable of the normal response to a depolarizing stimulus. In every aspect we have been able to test, the isolated cells behave as they do in intact tissue.

We feel that the single cell smooth muscle preparation has great potentialities. For the first time the cellular events in contraction can be observed not just before and after contraction, as was possible with fixed and sectioned material, but throughout a cycle of contraction and relaxation. Furthermore, use of whole cells instead of sections allows three dimensional observation of substructure which permits greater discrimination of changes in organization during contraction. There have been indications that there may be some organization of contractile components into fibrils or other definite patterns (Fig. 1). We are continuing to use single smooth muscle cells in dynamic studies of contraction recorded with microcinematography with the belief that such studies will greatly enhance the understanding of activation and contraction in vertebrate smooth muscles.

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Release of Oxytocin and Vasopressin by the Human Foetus during Labour

OXYTOCIN, a potent stimulant of myometrial activity, is used extensively in clinical practice for the induction of labour. The fact that in animals circulating concentrations of this peptide are increased during labour and maximal at the time of delivery[1,2] suggests that oxytocin released by the maternal posterior pituitary may play an important part in spontaneous labour. The role of endogenous oxytocin, however, has been disputed. Bioassays suggest that the circulating concentrations are increased to 100 μU/ml. or more[3,4], while indirect evidence suggests that there is no more than 10 μU/ml., and perhaps much less[5].

It is possible that the high estimates from bioassays in the human are due to non-specific factors, and preliminary data using a specific radioimmunoassay have shown that oxytocin in the maternal circulation does not usually exceed 1 μU/ml. (ref. 6). By contrast, oxytocin levels in foetal cord blood taken at the time of delivery are frequently raised[7], as are those of arginine–vasopressin (AVP)[8]. We have extended these findings, and now present evidence that oxytocin is released by the human foetus throughout labour.

Maternal and foetal blood samples were collected in cooled heparinized syringes and immediately separated at 4° C; the plasma was acidified to *p*H 1–2 before storage at −20° C (in which conditions there is no significant destruction of oxytocin by oxytocinase). Oxytocin and vasopressin were extracted and concentrated from plasma, and concentrations estimated by radioimmunoassay as described previously[7,9–11]. The assays have a maximum sensitivity of 0.75 μU/ml. for oxytocin and 4 μU/ml. for AVP. None of the materials known to mimic the effects of oxytocin in a biological assay has any effect. AVP shows less than 0.1% of the activity of oxytocin in the oxytocin assay, and oxytocin less than 0.025% of the activity of AVP in the vasopressin assay. The assays can detect exogenous hormone during infusion in normal subjects[7,11]. The oxytocin assay can detect infused oxytocin in pregnant women, and endogenous hormone in the plasma of goats at the time of delivery[7].

Oxytocin was undetectable in 81% of samples collected from a forearm vein of women in labour, indicating that concentrations were less than 0.75 μU/ml. (Table 1). In the 19% of subjects showing positive results the values ranged from 2–18 μU/ml. The sporadic appearance of oxytocin was not related to individual uterine contractions, and serial sampling showed that the presence of detectable concentrations was only transient.

Table 1 Plasma Levels of Oxytocin in Venous Samples obtained from Women during Labour

Stage of labour	No. of subjects	No. of samples	Samples containing detectable oxytocin (> 1 μU/ml.) No.	% of total	Oxytocin concentrations μU/ml.
1st	31	107	24	22	2–12 (mean 7)
2nd	74	74	9	13	2–18 (mean 9)

Oxytocin was detected in 76% of thirty-eight samples of umbilical arterial plasma collected at the time of delivery (Fig. 1). The mean level was 27 μU/ml. In paired umbilical venous samples oxytocin concentrations were lower, averaging 15 μU/ml. The arteriovenous difference was significant by Student's *t* test ($P<0.05$). Eight-four per cent of samples showed a positive arteriovenous difference. No oxytocin was detected in either the arterial or venous cord blood of an anencephalic.

In twelve out of sixteen cases of Caesarean section, maternal plasma contained oxytocin, the mean level being 12 μU/ml. When the patient was not in labour at the time of operation oxytocin averaged 7 μU/ml. in nine samples of umbilical arterial plasma, and 19 μU/ml. in paired samples of umbilical venous plasma (Fig. 1). When the patient was in labour the mean umbilical arterial level in four cases was 18 μU/ml. and umbilical venous levels 13 μU/ml. None of these differences was statistically significant.

Vasopressin was present in 90% of twelve samples of umbilical plasma collected at the time of delivery, the levels averaging 550 μU/ml. for arterial samples and 80 μU/ml. for paired venous samples (Fig. 2). This difference was statistically significant ($P<0.001$). None could be detected in the cord plasma of an anencephalic. At the time of Caesarean section umbilical arterial levels of vasopressin averaged 52 μU/ml. (arterial) and 21 μU/ml. (paired venous) in four cases when the patient was not in labour and 170 μU/ml. (arterial) and 32 μU/ml. (paired venous) in two cases in labour.

These results suggest that oxytocin release is only a sporadic occurrence in labour, and support earlier evidence that spontaneous uterine activity does not depend primarily on increased concentrations of oxytocin[1,6]. Three factors could negate this interpretation: (1) the free peptide might be inaccessible to the assay, if oxytocin circulates in bound or precursor form with release at the target organ; (2) the effects of transient release would be smoothed out if oxytocin is bound by the myometrium where it exerts a continuing action; (3) the levels of oxytocin required to stimulate labour may not be detected by the assay.

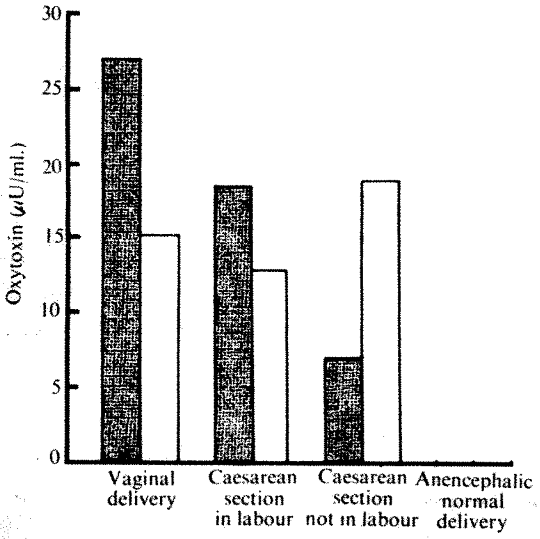

Fig. 1 Oxytocin levels in paired samples of foetal umbilical plasma collected at the time of delivery. The stippled areas indicate arterial levels, and the clear areas venous levels.

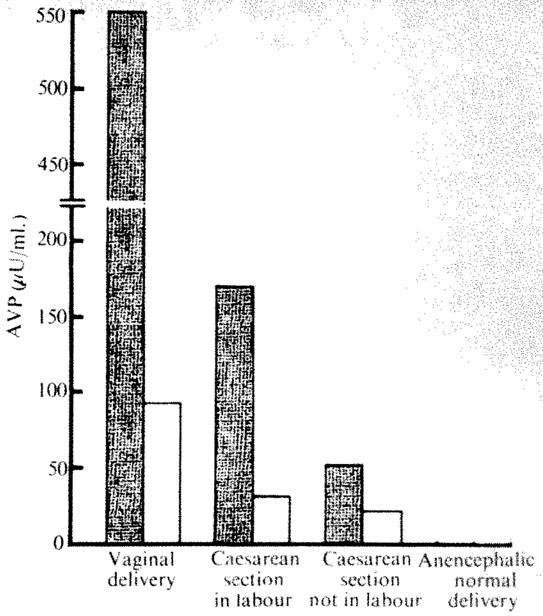

Fig. 2 Arginine–vasopressin levels in paired samples of foetal umbilical plasma collected at the time of delivery. The stippled areas indicate arterial levels, and the clear areas venous levels.

Larger concentrations of oxytocin and vasopressin were found in foetal umbilical plasma, suggesting that they originate from the foetal posterior pituitary. This was confirmed by the arteriovenous difference found in most cases, and by the absence of both oxytocin and vasopressin in the cord plasma of an anencephalic, in which there was no morphological evidence of neurohypophyseal tissue. The levels in samples collected at the time of Caesarean section suggest that the release of the hormones occurs particularly during labour. Thus, the arterial levels of oxytocin and vasopressin were greater when the operation was performed during labour than when performed as an elective procedure before the onset of labour.

The stimulus to the release of oxytocin and vasopressin from the human foetal pituitary is not known. A common denominator might be the stress and anoxia associated with delivery, or with the reduction in placental blood flow during contractions, or with the decrease in the functional reserve of the placenta which occurs during the last trimester. The significance of these peptides in the umbilical circulation is also unknown, though it is possible that they exert potent effects on the myometrium and the placental vessels[12]. It should be noted that the levels of vasopressin are among the highest recorded in any area of human physiology.

Previous workers have suggested that the foetal anterior pituitary may play a role in delivery[13–15]. Our results indicate that the foetal posterior pituitary may also be involved.

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Cytochalasin B Reversibly Inhibits Melanin Granule Movement in Melanocytes

AGENTS which cause metaphase arrest have been found to affect the rapid reversible darkening of frog skin under the influence of melanocyte-stimulating hormone (MSH)[1,2]. Darkening is caused largely by the dispersion of melanin granules in dermal melanocytes. After subsequent washing, the skin lightens and the melanin granules aggregate. In this system, preincubation with colchicine, colcemid, vinblastine or vincristine produces a slight increase in darkening induced by MSH, and a dosage-dependent inhibition of the subsequent lightening.

All these agents can bind the cytoplasmic protein that seems to form microtubules[3–8]. In melanophores of the teleost *Fundulus heteroclitus*, microtubules are aligned parallel to the direction of pigment movement, and persist whether the melanin granules are dispersed or aggregated[9,10]. Besides defining the channels in which the pigment moves, it is thought that microtubules may provide the motive force for pigment migration[9,10].

In considering the possible role of microtubules in such a motive force, the metaphase-arresting agents, applied to frog skin, are especially useful because their effects are unidirectional; they interfere with lightening of frog skin but not with darkening[1,2] (colchicine produces a similar effect in *Fundulus* melanophores[11]). These findings suggest that if a single network of microtubules is responsible for the movement of melanin granules in melanocytes and is disrupted by these agents, it would have to be involved in aggregation and not dispersion. An alternative suggestion[9] is that in *Fundulus* melanophores there are two interdigitating sets of microtubules with separate activation for aggregation and dispersion. In that case, however, one would have to assume that the microtubules involved in lightening are sensitive to metaphase-arresting agents while those involved in darkening are insensitive. Another alternative is that some other constituents of melanocytes are important for aspects of the movement of melanin granules in relation to microtubules, and suffice for dispersion but not for aggregation. Likely candidates for such a function are the contractile microfilament systems that are involved in motility of cells and within cells, and that are disrupted reversibly by the agent cytochalasin B[12–14]. The effect of this agent on the movement of melanin granules within melanocytes was therefore studied.

Frog skin was mounted on rings and soaked in Ringer solution to produce an aggregation of melanin granules which, if undisturbed, persisted for several hours. Changes in the state of dispersion of melanin granules were measured as changes in reflectance when the whole skin specimen, immersed in a beaker containing Ringer solution, was placed over a search unit attached to a photoelectric meter[1,15]. The reading of a given skin specimen after initial soaking was taken as the base line from which subsequent increases or decreases in reflectance were measured.

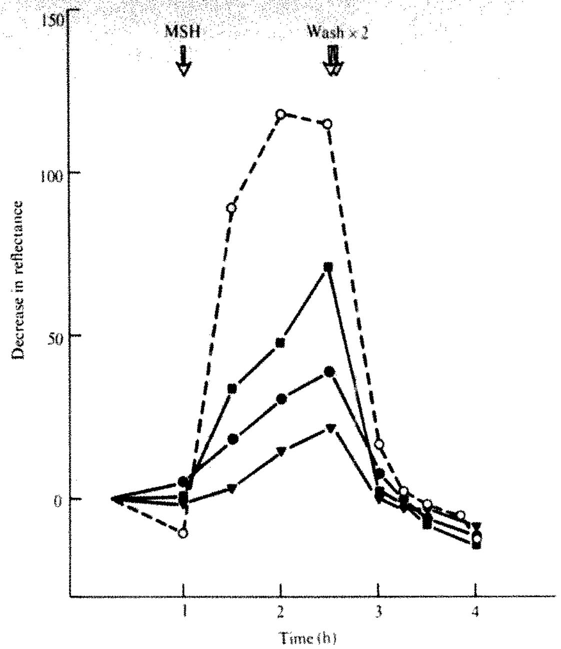

Fig. 1 The effect of cytochalasin B on darkening of frog skin, indicated by a decrease in reflectance. Each treatment group contained one skin specimen from each of four frogs[16]. Each point represents the total change in reflectance of the four specimens in that group. Specimens were incubated for 30 min in Ringer solution with or without cytochalasin B, then with MSH (0.5 U/ml.), and were then washed twice in fresh Ringer solution. ■, Cytochalasin B (1 μg/ml.); ●, cytochalasin B (5 μg/ml.); ▼, cytochalasin B (10 μg/ml.); ○, control.

When cytochalasin B (Imperial Chemical Industries Ltd) was added to this system 30 min before MSH (given by Dr A. B. Lerner, and prepared from a water extract of beef posterior pituitary powder (Armour) as described before[15]) there was a dose-dependent inhibition of subsequent darkening (Fig. 1). If the skins were then washed (by changing the Ringer solution), they lightened to a reflectance value near the base line. Controls and skins treated with only 1 μg/ml. of cytochalasin B consistently lightened at least to the base line; skins treated with higher concentrations seldom lightened completely within 2 or 3 h. If MSH was then added again (not shown in Fig. 1), all specimens tended to darken like controls. (Dimethyl sulphoxide (DMSO), in which cytochalasin B was dissolved (at 3 mg/ml.) before being diluted in aqueous media, has no effect on reflectance at similar dilutions.) Thus cytochalasin B seems to inhibit reversibly the dispersion of melanin granules that is induced within melanocytes by MSH.

When the skins were first darkened with MSH and their media then replaced by Ringer solution with or without cytochalasin B, there was some degree of inhibition of subsequent lightening (Fig. 2). If the same skins were then washed, those treated with low concentrations of cytochalasin B (0.5 μg/ml.) tended to lighten like controls; those treated with higher concentrations (for example, 5 μg/ml. in Fig. 2) tended not to return to base line during the period of observation. On subsequent stimulation by MSH, however, all specimens darkened like controls. Thus, in addition to its effect on darkening, cytochalasin B seems to have a less pronounced

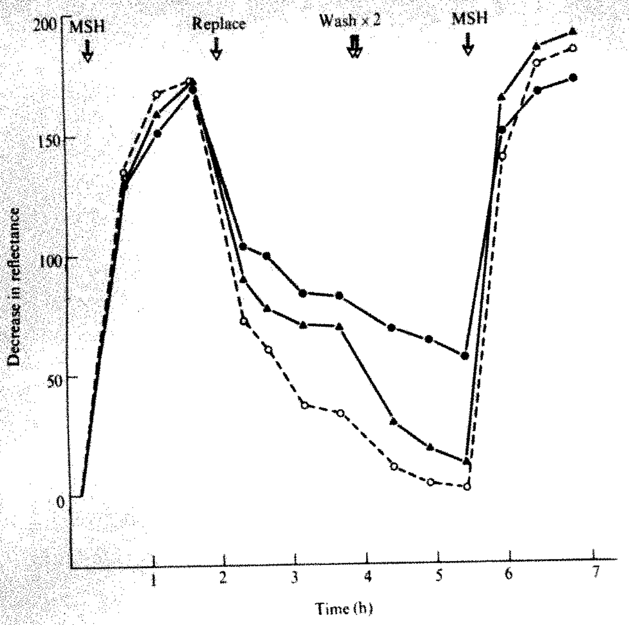

Fig. 2 The effect is seen of cytochalasin B on lightening of frog skin previously darkened by MSH. Specimens were incubated in Ringer solution with MSH (1.5 U/ml.), which was then replaced by Ringer solution with or without cytochalasin B. Later the specimens were washed twice, and still later they were again incubated with MSH. ●, Cytochalasin B (5 μg/ml.); ▲, cytochalasin B (0.5 μg/ml.); ○, control.

effect on the aggregation of melanin granules previously dispersed by MSH.

The interference of cytochalasin B in darkening and lightening of frog skin suggests that a contractile microfilament system is involved in the movement of melanin granules in melanocytes. In frog epidermal melanocytes—which are much smaller than dermal melanocytes and do not contribute significantly to changes in reflectance—melanin granules dispersed by MSH and then treated with cytochalasin B (20 μg/ml.) tend to aggregate, with marked reduction in the number of microfilaments seen (J. McGuire and G. Moellmann, personal communication). In specimens treated with high concentrations of cytochalasin B, the frequent failure of reflectance to return to base line is a secondary effect; such specimens, subsequently treated with MSH, darken like controls (Fig. 2).

A contractile system of microfilaments might provide the motive force for the movement of granules, particularly for their dispersion, while the integrity of microtubules seems also to be important for efficient aggregation. An investigation of the ultrastructure would be useful for further examination of these possibilities.

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Muscarinic Action of Acetylcholine

The muscarinic excitatory action of acetylcholine on central and peripheral neurones has been suggested to involve a reduction in membrane conductance for potassium ions[1,2]. This proposal was supported by observations that 2,4-dinitrophenol (DNP) could specifically suppress the excitation by acetylcholine of cerebral cortical neurones in the cat without affecting the excitatory action of L-glutamate, and that the hyperpolarization of these neurones by DNP involved an increase in the membrane conductance for potassium ions[3].

We report that the excitation of spinal Renshaw cells by a cholinomimetic which interacts with muscarinic receptors cannot be selectively reduced by DNP. The excitation of these cells by acetyl-β-methylcholine is very sensitive to atropine and is relatively insensitive to dihydro-β-erythroidine[4], and hence may be assumed to result from an interaction with muscarinic receptors. Experiments were performed on Renshaw cells of the seventh lumbar segments of cats anaesthetized with chloralose (60 mg/kg, intraperitoneal). Extracellular action potentials were recorded with the NaCl-containing central barrel of seven barrel micropipettes, and acetylcholine (bromide, 0.5 M), acetyl-β-methylcholine (bromide, 0.5 M), L-glutamate (Na salt, M, *p*H 7.5), DL-homocysteate (Na salt, 0.2 M, *p*H 7.5) and DNP (Na salt, 0.1 M, *p*H 9) were administered with suitably directed electrophoretic currents from aqueous solutions in the other barrels.

It was an invariable finding (seven Renshaw cells, five cats) that concentrations of DNP (anionic currents of 40–60 nA) which reduced the sensitivity of Renshaw cells to acetyl-β-methylcholine had a quantitatively similar effect on the sensitivity to acetylcholine, L-glutamate and DL-homocysteate. Concentrations adequate to completely block the action of the cholinomimetics also abolished that of the excitant amino-acids and spontaneous firing: such effects were often associated with a reduction in the amplitude of extracellularly recorded action potentials and were fully reversible. Although these results would be consistent with a hyperpolarizing action of DNP[3], which might reasonably be considered to diminish the apparent effectiveness of all excitants, the effect of DNP on Renshaw cells may be more closely related to processes involved in the generation of action potentials and hence also relatively non-selective towards excitants. Preliminary experiments indicate a similar, but not readily reversible, effect of iodoacetate.

Thus the effects of DNP on acetylcholine sensitive cortical neurones may not be directly applicable to the mechanisms of activation of muscarinic receptors on neurones elsewhere in the nervous system.

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Regulation of Adenosine 3′,5′-Cyclic Monophosphate Metabolism in Cultured Neuroblastoma Cells

MOUSE neuroblastoma C-1300 has a large number of electrical, biochemical and morphological properties characteristic of differentiated neurones[1-9]. The cell line is thus particularly useful as a model in which neuronal functions can be studied in a clonal propagating system *in vitro*.

The study of neurohormonal receptors in such cells is interesting, and both depolarizing and hyperpolarizing responses to acetylcholine have been noted[7,10]. We have investigated whether receptors in these cells were demonstrable by virtue of their ability to stimulate the accumulation of intracellular adenosine 3′,5′-cyclic monophosphate (cyclic AMP).

Clonal lines of neuroblastoma C-1300 derived by Dr T. Amano were grown routinely in Falcon plastic bottles in Dulbecco's modified Eagle medium, supplemented with 10% foetal calf serum, penicillin G (50 U/ml.) and streptomycin sulphate (10 µg/ml.), in an atmosphere of 10% CO_2 and 90% air. Cells were subcultured by brief incubation in a divalent cation-free medium (saline D_1[11] with 5.6 mM glucose and 59 mM sucrose to maintain isotonicity with growth medium). Cell lines were free of contamination by PPLO as determined by culture and by autoradiography following incubation with ^3H-thymidine (R. Dulbecco, personal communication).

For experimental study, cells were plated on 25 mm diameter glass cover slips and grown as described previously[12] for 5–6 days. Experimental incubations were performed in 2 ml. of medium minus serum at 37° C with an atmosphere of 90% air and 10% CO_2. Theophylline (1 mM) was present, except where indicated, during a preliminary 60 min incubation. Compounds to be tested were then added for 15 min of additional incubation, except where indicated. Finally, the medium was aspirated, the cells were fixed and the cyclic AMP extracted with 5% trichloroacetic acid (TCA). This technique is quantitative and seems to be virtually instantaneous. Cyclic AMP was analysed and assay specificity was verified as previously described[13]. Cellular material was quantified by determination of precipitated protein after solubilization in 0.2 N NaOH, by a modification of the method of Lowry[14]. An average cell sample contained 500 µg protein.

Table 1 Effect of Chemical Agents on Cyclic AMP Levels of Neuroblastoma Clones

Treatment	N4TG1	S20	N18	N10
	Neuroblastoma clone Cyclic AMP (pmol/mg protein)			
H_2O control	14	15	15	30
Isoproterenol, 10^{-4} M	13	14	20	28
Histamine, 10^{-4} M	14	13	21	30
5-Hydroxytryptamine, 10^{-4} M	14	15	18	31
PGE_1, 2.9×10^{-6} M	141	44	42	129
$PGF_{2\alpha}$, 2.9×10^{-6} M	19	16	18	36
Minus theophylline	26	13	13	36
Minus theophylline + adenosine, 10^{-4} M	28	13	13	38
H_2O control				36
Dopamine, 10^{-4} M				39
Carbamylcholine, 10^{-4} M				39

Four clonal lines of neuroblastoma have been found to have control levels of cyclic AMP ranging from 15–35 pmol/mg protein and have been tested with catecholamines, histamine, 5-hydroxytryptamine, adenosine, and prostaglandins E_1 and $F_{2\alpha}$ (PGE_1 and $PGF_{2\alpha}$) (Table 1). Only PGE_1 was found to be an effective stimulant, but it was active in all lines examined. One line (N10) was accordingly selected for further study, and in these cells responses to PGE_1 were independent of the cellular growth phase. This clone failed, in addition, to respond to carbamylcholine or dopamine.

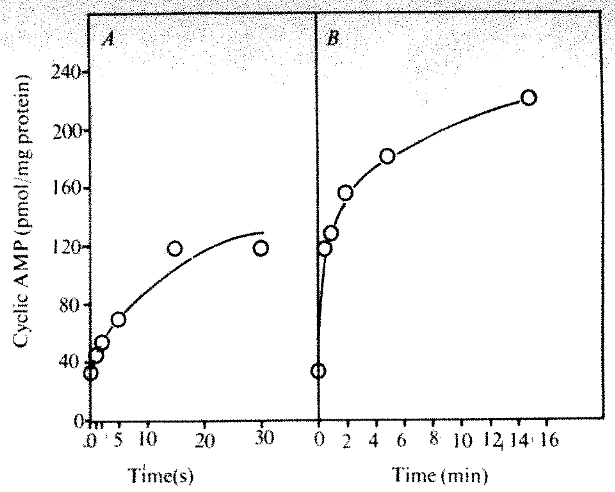

Fig. 1 Time course of response to PGE_1. For short incubation times (*A*), cover slips with adherent cells were dipped in beakers of PGE_1 (2.9×10^{-6} M) and then fixed in 5% TCA. For longer incubations (*B*), PGE_1 (2.9×10^{-6} M) was added to beakers containing cover slips and medium.

The time course of the effect of PGE_1 to stimulate cyclic AMP accumulation in these cells is shown in Fig. 1. The cover slip technique allows rapid manipulation of cell monolayers, minimizes diffusion time, and thus permits examination of short incubation times. Elevated intracellular levels of cyclic AMP were apparent after 1, 2 and 5 s of exposure to PGE_1. The rapidity of change of the total intracellular cyclic AMP content suggests that local changes of cyclic AMP concentration can occur with sufficient speed to mediate rather short latency effects of neurotransmitters. Maximal levels of cyclic AMP were attained by 5–15 min. While levels declined somewhat after 15 min (data not shown), cells maintained intracellular levels of cyclic AMP in excess of 100 pmol/mg protein 24 h after the addition of 2.9×10^{-5} M PGE_1 to growth medium minus serum.

The effects of PGE_1 concentration and of theophylline are seen in Fig. 2. Other data (not shown) indicate that responses seen at 2.9×10^{-6} M PGE_1 were nearly maximal. The PGE_1 concentration for a half-maximal effect is thus approximately

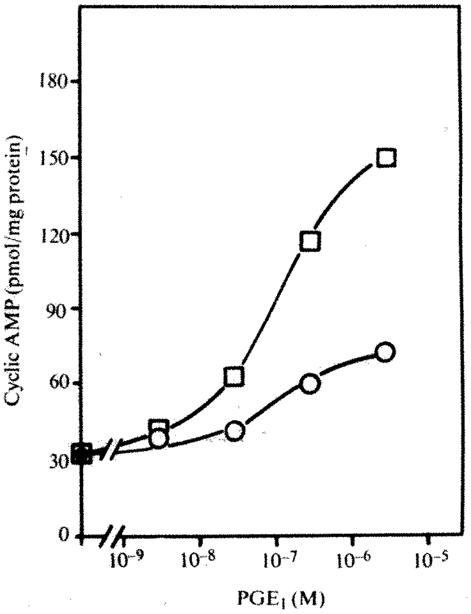

Fig. 2 Effect of PGE_1 concentration and theophylline. Cells were incubated for 60 min in the presence (□) or absence (○) of 1 mM theophylline. The indicated concentrations of PGE_1 were then added for 15 min of additional incubation.

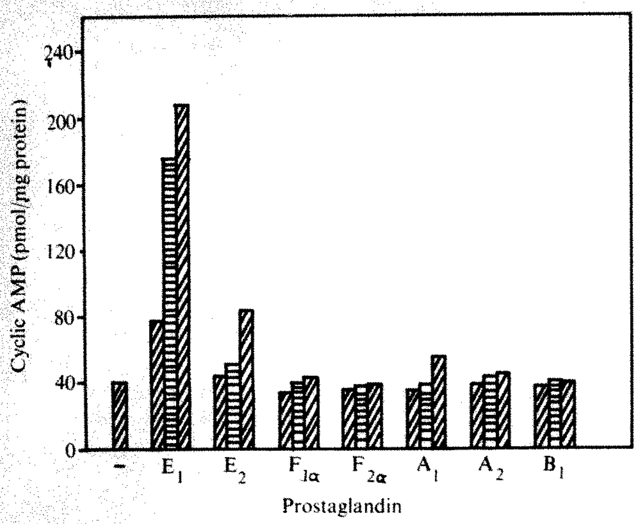

Fig. 3 Relative potencies of prostaglandins. Control level of cyclic AMP is shown by single bar to left. The indicated prostaglandins were tested at 2.9×10^{-8} M, 2.9×10^{-7} M, and 2.9×10^{-6} M (bars from left to right, respectively).

10^{-7} M. Theophylline (an inhibitor of cyclic nucleotide phosphodiesterase) potentiated the effect of PGE_1 two to three-fold, indicating that PGE_1 stimulates cyclic AMP synthesis.

The relative potencies of various prostaglandins are seen in Fig. 3. Prostaglandin E_1 was the most effective. PGE_2 showed definite activity at 2.9×10^{-6} M, and an effect of PGA_1 at 2.9×10^{-6} M was probable. Higher concentrations of these materials have not been tested.

The significance of the above data is two-fold. Prostaglandins have been shown to be released with neural activity and to have significant behavioural and other central nervous effects[15,16]. Their possible role as neurotransmitters has been discussed[15,17]. Prostaglandins of the E series have, moreover, been shown to antagonize the effect of norepinephrine to hyperpolarize and inhibit the rate of discharge of Purkinje neurones[18]. While direct evidence is unavailable, this effect of PGE_1 is presumably due to its ability to inhibit noradrenaline stimulation of the accumulation of cyclic AMP in this cell. Both inhibitory and stimulatory effects of prostaglandins on intracellular levels of cyclic AMP are, however, well known[19].

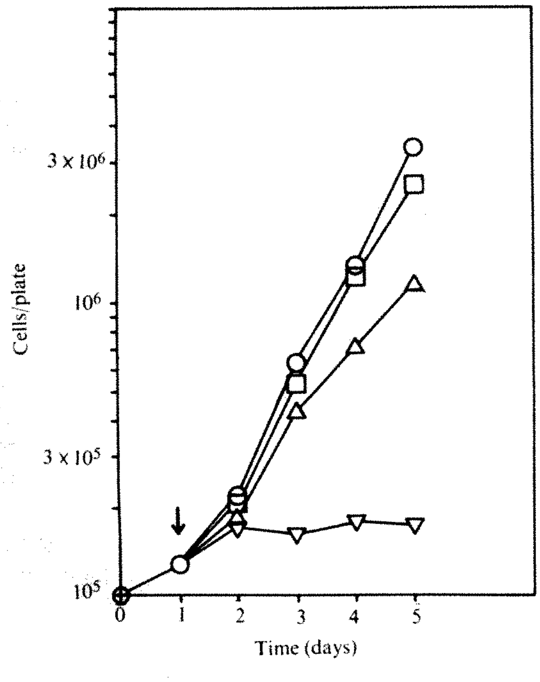

Fig. 4 Effect of PGE_1 and theophylline on cell division. Cells were plated at a concentration of 1×10^5 cells/60 mm dish. On day 1 compounds were added to growth medium as follows: growth medium alone (○); 1 mM theophylline (□); 1.5×10^{-5} M PGE_1 (△); 1 mM theophylline plus 1.5×10^{-5} M PGE_1 (▽). Medium was changed and drugs were added daily. Cell counts were performed on duplicate plates with a haemocytometer.

The stimulatory effect of PGE_1 on cyclic AMP levels allows one to produce both rapid and long lasting changes in the intracellular levels of the nucleotide in this model system. This ability should greatly facilitate the investigation of possible effects of the cyclic nucleotide on the differentiated neuronal properties exhibited by these cells. Many of the differentiated functions of these neuroblastoma cells, however, are expressed with far greater intensity when cell division is slowed at cellular confluency or by other means[4,5,9]. Before effects of PGE_1 or cyclic AMP on these parameters can be studied, it is necessary to evaluate their effects on cell growth. High concentrations of exogenous cyclic AMP have been shown to slow the rate of division of HeLa and other cells[20,21]. Pastan *et al.* have recently reported that dibutyryl cyclic AMP or PGE_1 inhibits growth of certain lines of fibroblasts[22].

Effects of PGE_1 and theophylline on the rate of cell division of neuroblastoma cells are shown in Fig. 4. After an initial lag, control cells grew logarithmically and doubled in less than 24 h. While theophylline alone had no effect on cell multiplication, PGE_1 inhibited markedly—only one-third as many cells were present on day 5 in 1.5×10^{-5} M PGE_1 as in control plates. The combination of PGE_1 and theophylline virtually prevented accumulation of cells. The two agents thus potentiated each other here, as also shown when cyclic AMP levels were examined (Fig. 2).

Our data show a stimulatory effect of PGE_1 on cyclic AMP accumulation in a neuronal tumour cell and represent, we believe, the first demonstration of an effect of any potential neurohormone on the cyclic AMP level of a defined cell of neural origin. In addition, effects on cell division such as those described suggest that factors regulating cyclic AMP levels may affect the course of cell differentiation or provide mechanisms for cell selection during development.

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Čerenkov Light from ^{32}P as an Aid to Diagnosis of Eye Tumours

THE ^{32}P uptake ratio test[1] as an aid to tumour diagnosis has had limited success for tumours in the posterior half of the eye[2–4]. Phosphorus is incorporated preferentially in dividing rather than non-dividing cells[5] and so, in essence, all the test requires is the oral or intravenous administration of ^{32}P orthophosphate (typically 100–500 μCi) and the β radiation from the lesion is measured and compared with that over the surrounding normal tissue.

In practice the test is complicated mainly by two factors. Inflammatory and certain other actively metabolic lesions will also incorporate ^{32}P in preference to normal quiescent tissue; and because β radiation has a short mean path length (3 mm in tissue), the placement of the detector is critical.

The problem of inflammatory lesions is largely overcome by spacing two observations of uptake to 4 and 24 h after administration of the isotope[4,6]. The inflammatory and metabolic components of uptake at 4 h greatly decrease by 24 h because of the rapid turnover of phosphorus in these processes. Thus one criterion reported for a positive diagnosis of malignancy[6] is that the uptake at both 4 and 24 h with respect to surrounding normal tissue has to be greater than a ratio of 1.5 : 1.

The placement problem is particularly acute when the test is applied to lesions posterior to the equator of the eye, for which surgery of access is most often necessary. Most eye tumours arise in this region in the choroid.

However, it is possible to detect the presence of ^{32}P in the back of the eye by observing the Čerenkov light produced by the passage of the β radiation in the vitreous humour. This can be done quite simply through the pupil using a highly sensitive photomultiplier tube.

From the theory of the Čerenkov effect it may be shown that the average radiation from ^{32}P in water will produce about thirty visible photons[7] per emitted β particle, and this has been used with transparent solutions of ^{32}P-labelled compounds in liquid scintillation counters[8].

I have investigated the use of this effect as a simple diagnostic test for the presence of ^{32}P in the posterior half of the eye. A specially selected bi-alkali type of photomultiplier tube was obtained (Centronic type 4249). This has a background emission of only 3 electrons/s from the cathode. It was coupled to a short length of 'Perspex' light pipe which was positioned over the eye of an anaesthetized rabbit, in contact with the cornea. When 0.8 mCi of ^{32}P was injected intravenously into the medial ear vein a signal of 400 pulses/s was produced from the photomultiplier tube. After a few minutes observation, a 0.0005 inch layer of black tape was placed over the end of the light pipe. The count rate fell to 80 pulses/s, which represented the fraction of Čerenkov light created in the light pipe by primary β irradiation. Thus the bulk of the signal detected by the photomultiplier tube can be attributed to Čerenkov light emanating from the vitreous humour as a result of the circulation of ^{32}P through the highly vascular choroid.

This test for Čerenkov emission should, therefore, provide a sensitive means of readily detecting and quantitating ^{32}P incorporated by ocular lesions and its applicability to the diagnosis of human ocular melanomata is planned.

Facilities and assistance for this work were provided by Dr H. A. S. van den Brenk of the Richard Dimbleby Cancer Research Laboratory, St Thomas' Hospital, and I am indebted to the research committee of the hospital for a grant to purchase the apparatus. The detector housing assembly was built by Mr A. Lee.

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Transfer of Blastocysts as Applied in Experimental Teratology

IT is well known that genetic constitution modifies the effect of teratogenic agents (Table 1). The most obvious example is the varying susceptibility of different strains of mice to teratogens such as cortisone, 6-amino-nicotinamide and salicylates[1–5]. In A/Jax mice, for example cortisone induces cleft palate in 100% of living embryos (if those with spontaneous cleft lip-palate—about 10% of births—are excluded). Isolated cleft palate can be induced with cortisone in only about 20% of embryos in other strains such as C57Bl and CBA[1,3].

Reciprocal cross differences demonstrated in the frequency of cleft palate induced by cortisone[3] or foetal death induced by salicylate[5] are matroclinous; the maternal influence could be chromosomal, cytoplasmic or uterine (Table 1). The maternal chromosomal effect would be transmitted with the *X* chromosome and the effect would thus be seen in the males, but cleft palate induced by cortisone is distributed equally among male and female embryos[3]. A cytoplasmic factor seems to be responsible for the differing susceptibility to 6-amino-nicotinamide in A/Jax and C57Bl mice[6], but Kalter could not demon-

Table 1 Genetic Factors modifying the Effect of Teratogenic Agents

Factors	Revealed by
1 Strain difference 2 Paternal influence 3 Maternal influence	Reciprocal crosses A × B B × A
(a) chromosomal	Increased risk in males
(b) cytoplasmic	Back crosses (A × B) × A (B × A) × A
(c) uterine	Egg transfer

strate such a cause of the susceptibility of A/Jax mice to cleft palate induced by cortisone[3]. The uterine environment is known to affect foetal growth[7]. By the technique of egg-transfer McLaren and Michie[8] demonstrated that the maternal effect on the number of lumbar vertebrae in mice was caused through the uterus. We have now investigated the possibility of transferring blastocysts in experimental teratology. The technique provides controlled experimental conditions, which cannot be obtained with time consuming back crosses.

Although the most common transfer method is to inject blastocysts into a free-dissected uterine horn (see review by Rafferty[9]), we chose a non-surgical technique[10], which we have modified. Three day old blastocysts (vaginal plug = day 0) were flushed from the uterine horn with Krebs Ringer solution and sucked from a watch-glass into a micro-pipette (Microcap) with an external diameter of 0.6 mm and maximum volume of 0.2 µl. A piece of a plastic tube was placed in the vagina as a speculum. Recipients were anaesthetized with a small intraperitoneal dose of a 2% solution of tribromo-ethanol (TBE); the blastocysts were expelled by gentle pressure into the horn. In addition to the transfer experiments reciprocal crosses were performed.

We knew that if cortisone is given intramuscularly during days 11, 12, 13 and 14 of gestation cleft palate is induced in 100% of A/Jax mice and in 12–20% of CBA mice[1]. Reciprocal crosses showed us (Table 2) that foetuses growing in an A/Jax mother developed a higher percentage of cleft palate than those in a CBA mother. There was no male dominance in the cleft palate groups, excluding the possibility of a pure *X*-linked inheritance. As the autosomal genome must be identical in the two crosses we have two alternative explanations—cytoplasmic factors, inherited through the egg, or uterine influence.

Table 2 Cortisone-induced Cleft Palate in Mice after Reciprocal Crosses

Mother		Father	Cleft palate (%)	Cleft palate (♀)	Cleft palate (No.)	Cleft palate (♂)	Litters (No.)
A/Jax	×	CBA	68	19	45	26	11
CBA	×	A/Jax	34	14	34	20	15

Cortisone, 62.5 mg/kg/day, was given intramuscularly on gestation days 11, 12, 13, 14.

Blastocyst transfer was controlled so as not to cause cleft palate in eighteen transferred A/Jax × A/Jax embryos to 11 CBA foster mothers. Homozygous CBA blastocysts were transferred to A/Jax foster mothers and *vice versa* (Table 3). As the recipients were mated with fertile males of their own strain, controls to the transferred foetuses were obtained within the same mother. Difference in eye pigmentation makes it easy to distinguish the two strains. The results, moreover, clearly demonstrate that transferred A/Jax × A/Jax foetuses are not protected in the CBA uterus; they all develop cortisone-induced cleft palate. Only 20% of CBA × CBA foetuses in CBA mothers had cleft palates. Even though only a few living CBA × CBA foetuses were transferred to A/Jax foster mothers, it was clear that there was no increase in frequency of cleft palate over the original 20%. Thus, the maternal influence observed in the reciprocal crosses cannot be interpreted as uterine.

Our modified technique of blastocyst transfer thus seems to be of value not only for studying the morphological malformations in the orthodox sense of teratology but also for problems more related to foetal pharmacology.

Table 3 Cortisone-induced Cleft Palate in Mice after Blastocyst Transfer

Genotype of embryos Transplanted	Genotype of embryos Controls	Mothers	Cleft palate (%)	Cleft palate (No.)	Litters (No.)
A/Jax × A/Jax		CBA	100	32	12
	CBA × CBA	CBA	20	11	12
CBA × CBA		A/Jax	22	4	12
	A/Jax × A/Jax	A/Jax	100	40	12

Cortisone, 62.5 mg/kg/day i.m., on gestation days 11, 12, 13, 14.

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Transformation of Human Leucocytes by Throat Washing from Infectious Mononucleosis Patients

A SIMPLIFIED procedure for studying induced transformation of human leucocytes *in vitro*[1] utilizes umbilical cord blood leucocytes which are easily obtained and do not transform spontaneously. When treated with cell-free filtrates from lymphoblastoid cell lines of a mononucleosis patient and three healthy persons, cord blood leucocytes were transformed to rapidly and persistently multiplying lymphoblasts[2,3]. Chemical carcinogens and ionizing radiation were ineffective[2]. In a long term search for transforming agents in the human environment, we have studied numerous agents including the secretion from upper respiratory tract of mononucleosis patients. We found that their secretion contained transforming activity.

Infectious mononucleosis was diagnosed on criteria proposed by Hoagland[4]. Secretion from the upper respiratory tract of eight patients was collected by gargling with 10 ml. of tissue culture medium[1], 5 to 17 days after onset of illness. Throat washings were filtered through a 0.45 membrane filter and the filtrate stored at below −60° C until use.

Umbilical cord blood leucocyte suspension, 5×10^6 leucocytes/ml. of nutrient medium, was prepared[1] and 0.5 ml. of filtered throat washing was mixed with 1 ml. of leucocyte suspension. Uninoculated leucocyte cultures from the same specimen of cord blood were similarly treated as control.

Four of the eight throat washings had transforming activity, evidenced by the ability to induce the formation of large aggregates of small round cells and increase in the number of viable cells as early as the third or fourth week after inoculation. Transformed leucocytes resembled lymphoblasts in appearance and multiplied rapidly and persistently. All four transformed cultures have been subcultured twenty-two times at intervals of 3 or 4 days, and are still growing actively. As expected, the eight uninoculated control cultures were not transformed. The experiment was repeated with the four positive throat washings and these also had transforming activity.

The transformed leucocytes were assayed three times for Epstein-Barr virus (EBV) antigen by the indirect immunofluorescent test[5], but the results were inconclusive as all transformed cultures contained γ globulin-secreting cells.

The importance of our work is that it is the first detection of a leucocyte-transforming agent, which must be considered potentially oncogenic for man, in human upper respiratory tract secretion. Further investigation into the nature of this transforming agent may clarify its relationship with (*a*) EBV, (*b*) transforming agents from various lymphoblastoid cell lines (from Burkitt's lymphoma[6,8], acute leukaemia[7], mononucleosis patients[2], and healthy persons[3]) and (*c*) the filtrable agent which can convert lymphoid cells from negative to positive for EBV antigen[9].

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Salmon Nomenclature

Payne, Child and Forrest[1] have shown little regard for the rules of zoological nomenclature in proposing the subspecific names "*europaeus*" and "*americanus*" for the Atlantic salmon, *Salmo salar*. First, the European stock, binominally named by Linnaeus, must become the nominate subspecies and, therefore, should bear the name *Salmo salar salar* Linnaeus, 1758[2] rather than *S. salar europaeus*. Second, a cursory examination of the literature reveals a number of older and available names for the North American stock. These include *S. immaculatus* Storer 1950[3], *S. sebago* Girard 1854[4], *S. gloveri* Girard 1856[5] and *S. ouananiche* McCarthy 1894[6], any of which must take precedence over *S. salar americanus*. Undoubtedly any British ichthyological systematist could advise the authors on correct choice of names for their subspecies. At the same time, they should consider that while designation of type-specimens in the species group is not mandatory, it is a protocol to which systematists almost invariably adhere[7].

Although the authors are aware of "communal feeding grounds off Greenland" for both European and South American salmon stocks, they seem to be unaware that some salmon spawn in Greenland[8]. The transferrin type of this Greenland stock is apparently unknown, but could be intermediate between the European and American stocks. Furthermore, the small size of their North American sample (only seventy-eight specimens) from a geographically restricted area is hardly comparable with the large sample from the British Isles (4,414 specimens). Perhaps the authors would be advised to test their hypothesis on a larger sample from North America as well as samples from Greenland and European localities other than the British Isles before they take the step of proposing corrected subspecific names for these salmon stocks.

Finally, however, they are only able to distinguish 57.7% (forty-five out of seventy-eight specimens) of their North American sample from their European sample. Few taxonomists would agree that such a low percentage discrimination deserves subspecific designation.

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Drs Payne, Child and Forrest write: Dr Gruchy's criticism of our proposed nomenclature is quite valid and we accept that the European subspecies of the Atlantic salmon should be called *Salmo salar salar* L. according to the International Code of Zoological Nomenclature. The choice of a correct name for the North American stock is more difficult in view of the complexity of earlier terminology and a detailed study of the literature is indicated.

Our thesis is that free gene exchange was possible through the amphi-Atlantic range of *S. salar* until the end of the Last Inter-Glacial when the expansion of the polar ice-cap caused a major discontinuity in the range. We believe that genetic contact has never been re-established as shown by the restriction of the transferrin variants Tf3, Tf4 to North America and Tf2 to Europe (one must assume that *Tf1* was the "ancestral" gene at this locus and that *Tf2*, *Tf3* and *Tf4* have arisen by mutation at this locus since the establishment of a geographical barrier in the polar region of the North Atlantic). We do not conceive of these transferrin variants as definitive characters for the recognition of morphological subspecies but as indicators of the existence of a major discontinuity in the free exchange of genetic material through the species. However, we hope that absolute discriminants may be discovered from further work.

An analysis[1] of 1,623 Atlantic salmon sera collected over the area between Labrador and Maine showed that there is a widespread polymorphism in transferrin phenotype which is determined by three allelomorphic genes. It is highly probable that these alleles correspond with *Tf1*, *Tf3* and *Tf4* described in our paper. This work confirms that the transferrin polymorphism we describe in the salmon populations of the Gulf of St Lawrence is not a feature applicable only to this geographically restricted area.

We have not examined material from the very small native population in Greenland. However, an analysis of more than 1,000 sera samples from the drift-net fishery in the Davis Strait between West Greenland and Canada did not reveal any intermediate phenotypes (Tf2/Tf3, Tf2/Tf4). We have examined a small sample (100 specimens) from rivers in SW Iceland; all these fish had the Tf1 phenotype. While further work in this area is required, this must be taken as provisional evidence that the *Tf3* and *Tf4* alleles have not spread from North America into the European side of the North Atlantic via Greenland.

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GENERAL

Balancing Mutual Force Reductions

THE problem of reducing conventional forces in the European setting in a balanced manner as between the forces of the NATO and Warsaw Pact countries is of some political interest. Here I set out to provide logical baselines, using a mathematical approach but without indulging in massive computation, for deciding when, and in what sense, small force reductions involving two opposing parties might be said to be balanced. Three different approaches to the question are made, each based on essentially different but plausible idealizations of what balanced reductions in military strength may mean, or may be taken to mean by the parties concerned.

This first approach begins by assuming that there is, before any reductions, a balance between the two parties, A and B, and that this balance can be represented in general by an equation of the form

$$g(M_A, T_A, P_A, N_A, \ldots) = f(M_B, T_B, P_B, N_B, \ldots.) \qquad (1)$$

where g and f are the war-fighting capabilities of A and B respectively, and are functions (unknown) of the respective numbers of troops (M), tanks (T), aircraft (P), tactical nuclear weapons (N) and so on deployed by each side. From equation (1), for small reductions in troops, say, ΔM, it follows that

$$\Delta M_A/\Delta M_B = \partial M_A/\partial M_B \left(\text{and } \frac{\Delta T_A}{\Delta T_B} = \frac{\partial T_A}{\partial T_B} \text{ and so on}\right) \qquad (2)$$

and we can say that the reductions, $\Delta M_A/\Delta M_B$, are balanced when equation (2) is satisfied.

It is convenient to proceed by making the further assumption that the existing level of forces came about as the result of an arms race, fitting either the well known but crude Richardson model[1], or some modern variant of it such as Caspary's[2], and which has reached a stage of zero growth rate in the armaments expenditure of both sides.

For zero growth rate in expenditure both the Richardson and the Caspary models reduce to the simple form

$$M_A \doteqdot kM_B \qquad (3)$$

where k is a dimensionless constant incorporating the Richardson constants[1] and a factor translating financial expenditure into troop levels (the equation is inexact because of the assumption, very nearly correct, that recurring expenditure on each side of the European conventional military confrontation is predominantly, directly or indirectly, on manpower)

Combining equations (2) and (3) now gives

$$\Delta M_A/M_A \doteqdot \Delta M_B/M_B \qquad (4)$$

and assuming that the ratio of tank numbers to troop numbers within a fighting force should remain approximately fixed, it follows from equation (4) that

$$\Delta T_A/T_A \doteqdot \Delta T_B/T_B \qquad (5)$$

Thus within the meaning of balance as it has been understood in this section it seems that for small ground force reductions to be carried out in a balanced way they should take the form of equal percentage cuts.

The second approach assumes not only that there is a balance but also that this balance is stable in the sense that an outbreak of hostilities would lead to no advantage, initially at least, for either side. Small peacetime reductions in forces related in the same way as those that might be expected to occur in the earliest stages of an outbreak of hostilities are then said, in the sense of the term as used here, to be balanced.

If, first of all, we treat the initial outbreak of hostilities for the sake of simplicity as a tank battle, the least complicated equations which seem to satisfy the more obvious requirements of a representation of respective tank losses on the outbreak of hostilities are

$$\begin{aligned} \mathrm{d}T_A/\mathrm{d}t &= -pT_AT_B + R(t) \\ \mathrm{d}T_B/\mathrm{d}t &= -qT_AT_B + S(t) \end{aligned} \qquad (6)$$

where R and S are reinforcement functions of time (t) measured from the outbreak of hostilities and which tend to zero as t tends to zero; and p and q are measures of the "killing" rates of the tanks of B and A respectively.

Putting t equal to zero equations (6) give approximately for the tank losses ΔT_A and ΔT_B

$$\Delta T_A/T_A = p/q \; \frac{\Delta T_B}{T_B}\left(\frac{T_B}{T_A}\right) \qquad (7)$$

At this stage a further assumption needs to be made concerning the scenario for the tank battle: this is that the numerically larger tank force (let us say T_A) is taken to be the attacker. It is then possible to ascribe a value to p/q because it is fairly generally accepted[3] that tanks can more effectively destroy other tanks from a defensive position than the other way round. If the current NATO tank strength in the NATO Northern and Central Theatres of Europe is assumed accurately to reflect this superiority of the defence in the sense that $p/q = T_A/T_B$, then equation (7) becomes

$$\Delta T_A/T_A = \Delta T_B/T_B \qquad (8)$$

If, however, p/q is taken to be a fixed ratio derivable from the study and observation of historical conflicts and weapons trials, and Ogorkiewicz seems to put its value at around 4 in this context[3], then equation (7) becomes

$$\Delta T_A/T_A = 4\; \Delta T_B/T_A\; (T_B/T_A) \qquad (9)$$

Inserting the ratio T_B/T_A of the current NATO to Warsaw Pact tank forces in the Northern and Central Theatres of Europe[4] equation (9) now becomes

$$\Delta T_A/T_A = 1.6\; \Delta T_B/T_B \qquad (10)$$

Alternatively the outbreak of hostilities can be represented in a more general way if we accept Lanchester's theorem[2,5] that the "fighting strength" of a force is proportional to the square of the number of units of that force. If we can take it that the condition that the outbreak of hostilities leads to no initial advantage for either side can be met by equating the initial "fighting strengths" of each side, then according to whether we view the outbreak of hostilities as a troop engagement with tanks as firepower or as a tank battle supported by troops, we have

$$M_A^2 = uM_B^2 \qquad (11)$$

or

$$T_A^2 = vT_B^2 \qquad (12)$$

where u and v are dimensionless constants. From equations (11) and (12) for small losses ΔM in troops and ΔT in tanks we obtain

$$\Delta M/_A M_A = \Delta M_B/M_B \qquad (13)$$

$$\Delta T_A/T_A = \Delta T_B/T_B \qquad (14)$$

Thus for small peacetime reductions in tank forces of the NATO and Warsaw Pact alliances in the Northern and Central Theatres of Europe to be balanced in the sense of the term used here they must lie somewhere between the equal percentage reductions suggested by equations (8) and (14), and percentage reductions approximately in the ratio 3 to 2 in favour of the smaller force according to equation (10). Troop reductions, using the arguments of the prevous section fortified by equation (13), should be within the same range of proportions.

Finally, the existing disposition of forces may be in balance in the sense that both sides A and B perceive the existence of a situation of mutual deterrence, each side being convinced that a surprise attack by either will leave intact too large a proportion of the original fighting strength of the defender (his second strike force) to make the attack worthwhile. For conventional forces the problem of what then constitutes balanced peacetime reductions is most easily handled in terms of tactical air strength.

Assuming for the moment that both A and B will, plausibly, regard peacetime reductions in numbers of aircraft as balanced when they leave the existing expected ratio of second strike strengths unaltered, we can find an expression for this ratio if we can write the numbers of second strike aircraft as P_A^0 and P_B^0 where

$$P_A^0 = P_A(1 - c_A)^{f_B P_B p_A/P_A} \tag{15}$$

$$P_B^0 = P_B(1 - c_B)^{f_A P_A p_B/P_B} \tag{16}$$

and P_A,P_B are the existing numbers of aircraft; c_A,c_B the probabilities that on average p_A and p_B aircraft will be destroyed before take off by one aircraft of the forces of B and A respectively; and f_A,f_B are the fractions of the airforces of A and B devoted to a first strike disarming attack.

Then dividing equation (15) by equation (16) and differentiating we obtain after some manipulation

$$\mathrm{d}P_A/\mathrm{d}P_B = P_A/P_B \tag{17}$$

which becomes, after equating the small peacetime reductions in aircraft numbers ΔP_A and ΔP_B to the differentials,

$$\Delta P_A/P_A = \Delta P_B/P_B \tag{18}$$

from which and from equations (15) and (16) it also follows that

$$\Delta P_A^0/P_A^0 = \frac{\Delta P_B^0}{P_B^0} = \Delta P_A/P_A \tag{19}$$

Thus not only are reductions in numbers of aircraft balanced in the sense of this section when they are carried out in equal percentages according to equation (18) but also, provided they are accompanied by numerically equal percentage reductions by both sides in troops and tanks, the new, smaller second strike tactical aircraft forces will automatically be in the same ratio to the new number of military targets (troops, tanks and aircraft) possessed by the other side as are the existing second strike forces to the existing number of military targets. (This will not be precisely true since there are second strike targets for tactical aircraft, such as bridges, fortifications and certain townships, the number of which will scarcely, or only indirectly, be affected by reductions in military equipment and personnel.) This important result clarifies and supports the original assumption that tactical aircraft reductions which preserve in being the existing ratio of second strike forces could be taken as balanced by the parties involved.

As a prescription for the way in which "balanced" force reductions in Europe should be carried out this paper does not pretend to completeness. In particular it does not deal with the question of how large such reductions should be, only their inter-relationships, although the technique of analysis is usually based on a presumption of small, up to 10%, reductions.

This article sets out to put the case for equal or near equal percentage cuts as being most likely to preserve the existing balance of conventional military strength, over the wide spectrum of meanings given to that phrase. And the plausibility of this proposition gains considerably from the consistency with which it emerges from the three approaches to the problem.

Work on an extended version of this article is in progress. I thank R. P. Barston and R. N. Fournier for valuable conversations.

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Supernatural Beliefs of Graduate Students

IN their recent report entitled "Supernatural Beliefs Among Graduate Students at the University of Pennsylvania"[1], Salter and Routledge examined the hypothesis that further education leads to a decline in supernatural beliefs, an idea already tested in a population of undergraduate males[2]. Their sample, however, was strongly biased in favour of male students with one year of graduate study and limited to married students living in a university campus residence hall, and therefore was unrepresentative of the total graduate student population. Of the 9,000 graduate students, approximately 50% are married and, of these, only 10% live in university campus housing.

We doubt the precision of the method used to measure the extent of an individual's belief in the supernatural. Each subject was rated on a scale from 0 to 20 according to his assessment of strength of his belief in certain phenomena. It is not clear if he was rated by himself or by the interviewer. Zero indicated total unqualified disbelief, 10 indicated neither belief nor disbelief, and twenty indicated total unqualified belief[2]. This rating could not be used to meaningfully compare different individuals, nor does the same score in different categories suggest an equivalent level of belief. For example, the authors would propose that a score of 20 for belief in the power of prayer has an equivalent relationship to the Gestalt of supernatural belief as does a score of 20 for belief in unidentified objects (UFOs). Similarly, a score of 10 on UFOs might suggest either an open mind on the subject of extra-terrestrial life, or an intermediate level of belief in something supernatural.

The most egregious errors, however, were in the analysis. Salter and Routledge, as well as the previous workers they cited, assumed that their scores represented interval rather than ordinal measures. That is, they assumed that a score of 10 on a particular item represented twice the belief as did a score of 5. There is no basis whatever for this assumption, as their 20-point scale was an arbitrary one. They calculated, however, the means of the scores for each of their eight items (astrology, ESP and so on), an operation which is invalid for ordinal data.

They then tested the hypothesis that amount or field of education decreases supernatural belief by measuring concordance of year or of field of study with the mean scores of the eight items. Their method of testing these hypotheses assumed, for example, that both belief in prayer and in UFOs were, in some sense, equivalent components of supernatural belief, and, therefore, that the scores on each should be concordant. Yet, as discussed, this is an unreasonable assumption. Their failure to find significant Kendall coefficients of concordance could have been as much due to true lack of concordance among the (mean) scores of the various items, as to the absence of trends in these items over years or fields of graduate study.

Finally, the authors made a number of contradictory assertions. For example, they write: ". . . natural and [*sic*] biological scientists had the highest mean belief scores and students in the arts . . . had the lowest. . . . These differences [were] insignificant . . .". Furthermore, descriptions of procedure were vague: "Our interviewers were instructed to explain the questions if problems arose", and the authors remark without additional comment: "Cell frequencies do not in every case add to the total because some data were improperly transcribed".

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BOOK REVIEWS

Logical Development

Development of Mathematical Logic. By R. L. Goodstein. Pp. vii+150. (Logos: London, September 1971.) £3.50.

WHEN Boole applied algebraic techniques to logic in 1847, he was thinking of logic in the traditional manner, as the theory of correct inference; and both Frege and Russell also confined their attention to such subject matter when they sought to exhibit logic as the ultimate foundation of pure mathematics. But as mathematical logic entered its classical phase, during the 1930s, other studies were seen to be very much bound up with it, as for example recursive arithmetic. Today we find mathematical logic firmly established as one of the central mathematical disciplines, ramifying in many different directions, for example into mathematics proper, foundations of mathematics, and the theory of computation. Many good books on mathematical logic are now available, written at all levels of difficulty, and varying between complete informality and austere formal rigour of presentation; but it is not altogether easy to get from any one of them an overall view of the entire field. This is precisely what Professor Goodstein's remarkable book provides.

The book begins with four chapters on propositional and predicate logic, treated both by model theory and by proof theory (that is, both semantically and syntactically). But these chapters are not as in most other books, since very many special topics are touched upon, such as Post's theorem on Sheffer functions, intuitionist calculi, natural inference and tableaux, sequent logic and Kripke semantics. There then come four more chapters, devoted respectively to recursive functions, formalized arithmetic, free-variable arithmetics, and axiomatic set theory, with an even greater wealth of special topics—and all this in 150 pages, which include a well chosen bibliography!

It seems to me that beginners would tend to find much of the book hard, and perhaps rather bewildering, since so many big topics are reported on in summary fashion, accurately indeed, but without much explanation. To the reader who already has some initial knowledge of the whole field, however, the book could prove invaluable, both as a means of orientation and as a guide to further topics that it is important to learn something about. Anyone who worked through the book systematically, reading up each topic in turn with the aid of the notes and bibliography, would find himself committed to an extended course of study; but by the end of it he would really understand what modern mathematical logic, taken in an all-embracing sense, is about. He might not have studied automata theory, say, and perhaps a few other things, but his reading would have been thorough and productive.

G. T. KNEEBONE

US Science

Science in American Society: a Social History. By George H. Daniels. Pp. xii+390+x. (Alfred A. Knopf: New York, May 1971.) $10.

THIS well written and amply documented book is largely about the period before 1900. Only the last and part of the penultimate chapters cover the present century, making this another case of *Hamlet* without the Prince. The time focus is all the more regrettable because of the promise of the subtitle and the author's politely polemical preface, a promise largely unrealized even in the treatment of the earlier period. Promise and performance do not match; why they do not match endows this book with some historiographic interest.

Daniels bluntly characterizes much of the writings in the history of science as "celebratory", presumably of great men and great achievements or as being an idealized, if arid, analysis of scientific ideas. Science as a human activity, Daniels insists, occurs within a national ideological framework, and is best viewed as a part of a national culture. The part influences the whole, while the whole influences the part. While Daniels stops short of asserting that science as practised in one nation is inevitably different from the practices in another nation, the book is definitely in the old tradition stressing America's historical uniqueness.

Among historians of science at present is a rather lively stirring about the shape of the subject. Voices are heard asserting the importance of factors outside the internal flow of scientific data and concepts. Coming to mind immediately, is the recent spate of articles on the origins of the Royal Society. In this rather academic discussion the United States is unique, for only there, to my knowledge, do we find a substantial body of historians investigating the sciences as part of the national experience, rather than particular disciplines. These historians—at least twenty-four come to mind—are, for the most part, not close to their colleagues in the history of science proper, being concerned with governmental policies, scientific organizations and informal groupings; the applications of science to medicine, agriculture, and technology; the relations of scientists with other groups in the United States; and (recently) the socio-economic origins of the scientific community. They are best described as general American historians trying to integrate the sciences into the national history.

Daniels seems to belong to this school; parts of the text are explicitly derived from such writings, including his own contributions. But the volume is far from social history. It is, rather, from a different genre, that of American intellectual history. The method is closer to Perry Miller, Henry Steele, Commager or Ralph Gabriel than to Marc Bloch. What we have here are idealized abstractions—Newtonianism, Darwinism, the Progressive Era, the Jacksonian Spirit — around which Daniels arrays what scientists and non-scientists said about science. Although the genre is worthwhile, it hardly constitutes a social history. Only his nationalistic focus prevents Daniels from realizing that his practice is closely related to many writings of conventional historians of science. A real social history of science is sorely needed. Large stretches of the literature are either too close to a pedantic antiquarianism or too idealized. Whatever the relationships between the content of science and the ambient milieu, we sorely need a full picture, not a partial view, of the totality of scientific activity.

What strikes an American reader is how Daniels, in spite of his virtues, runs into trouble because programme and practice fail to match. Daniels strongly insists—too strongly in my opinion—that a democratic culture concept in the pre-Civil War years hindered professional growth by an anti-elitist, egalitarian view of science. By the Progressive Era, the expert is in the saddle for reasons left unclear by the author. Since his method inclines to neat intellectual dichotomies, Daniels equates uniformitarians with partisans of natural selection and catastrophists with opponents of natural selection, a gross oversimplification of the situation in the United States and Britain. Being conscious of intellectual positions, Daniels cites chemists in post-Civil War America as leaders in the pure science ideal drive. A social history would have noted that many, perhaps most, chemists of that day were in applied endeavours. Since intellectuals wrote about the survival of the fittest, Daniels assumes businessmen literally believed in this competitive ideal, even though he himself cites the contrary views of Andrew Carnegie. Most American historians today note that many American businessmen tried their best to minimize competition by forming trusts or engaging in tacit price fixing. Daniels is unaware of recent work casting doubt on the view that the Social Darwinists believed in the jungle bloody survival of the fittest.

A sprinkling of errors indicates a rather careless handling of mere facts, even for intellectual history. Cartier did not explore western Canada. Benjamin Rush studied chemistry at Edinburgh to get a medical degree, not merely to aid industry. The Smithsonian was not a "museum of public entertainment" in its early years. Two different dates are given for the start of the important Darwin–Gray correspondence. Darwin was by no means one of the first scientists to appeal to nature rather than to logic. There never was a Federal Bureau of Agriculture, the term "Department" being used even before cabinet status was attained. Simon Newcomb never "headed a government observatory". John Wesley Powell fell in the early 1890s, not the late 80s. The Science Advisory Board of 1933 was not advisory to the Tennessee Valley Authority. Frank B. Jewett was president of the National Academy of Sciences, not the AAAS. While these are perhaps pedantic quibbles in terms of that splendid abstraction, a national ideological framework, yet they are the stuff from which a true social history of the sciences in America will some day emerge.

NATHAN REINGOLD

Substitution Reactions

Free Radical Substitution Reactions. By K. U. Ingold and B. P. Roberts. Pp. viii+245. (Wiley: New York and London, August 1971.) £5.75.

THE authors of this volume seem to have found considerable difficulty in finding a suitable title. Having chosen *Free Radical Substitution Reactions*, they take justifiable pains to make clear what is not to be found in the book. The subtitle brings the prospective reader much nearer to the real content, which is concerned with S_H2 reactions. If the reader is still mystified the preface makes the position quite clear in the statement that bimolecular homolytic substitution reactions involve the attack on an atom in a molecule by an incoming radical to bring about replacement of a second radical originally bound to the atom. Further, since the majority of the chemical elements are multivalent, the atom under attack is not a terminal one. Ten chapters deal in turn with elements of group IA, groups IIA and B, group IIIA, group IVA, group VA, group VIA, group VIIA, transition elements, rare earth elements, and finally group O elements, for which, incidentally and not surprisingly, no example of an S_H2 reaction is as yet known. The chapters vary considerably in length and, as is to be expected, reactions at the oxygen atom receive the most attention. Reactions at carbon, sulphur, phosphorus and the metals tin, mercury, cadmium, zinc, magnesium, and aluminium are also reported at some length. The presentation of the subject matter is logical and precise to the extent that the reader should be able quickly to locate the information he wants and for this reason a subject index is not included.

The subject matter concerns bimolecular homolytic processes at multivalent atoms involving attack on interior or non-terminal atoms. Such reactions may be synchronous or stepwise, depending in each case on the properties and behaviour of the initially formed adduct radical. Where appropriate, stereochemical considerations are fully discussed. Reactions involving metals, for example, magnesium, mercury and tin, frequently have important implications for preparative processes. In some of the reactions discussed the existence of an S_H2 reaction is by no means firmly established, as is in fact made quite clear by the authors themselves, and there is frequently quite a divergence between the behaviour of reactions at atoms within the same group, for example, nitrogen and phosphorus. The wide occurrence of S_H2 reactions at oxygen is not unexpected. Such processes have attracted much attention largely as a result of the use of peroxides as initiators in polymerization studies and other free radical processes. Reactions at the sulphur atom have also received wide study in particular with compounds containing the relatively weak sulphur–sulphur bond. The subject matter is treated with a measure of critical insight into mechanisms and perhaps one of the most interesting features of this volume is to be found in the revelation of the diversity of behaviour which is to be found in the reactions which can be classified as S_H2 processes.

This volume makes a useful addition to the rapidly growing literature of free radical chemistry and it is particularly acceptable because it brings together for the first time a wide range of information, which will become of increasing interest to both academic and industrial chemists.

D. H. HEY

Mathematical Genetics

Probability Models and Statistical Methods in Genetics. By Regina C. Elandt-Johnson. Pp. xviii+592. (Wiley: New York and London, August 1971.) £11.75.

THIS book covers the standard topics of mathematical genetics, such as segregation ratios, gene frequencies in populations, genetic correlations, the effects of selection, inbreeding, linkage, mutation, assortative mating and so on. It also includes a chapter on the theory of incompatibility of transplants, a field in which Professor Elandt-Johnson has herself done some useful work. The author states that the book is intended for biologists with only a minimum knowledge of mathematics and statistics; about six of the nineteen chapters are taken up with an explanation of standard statistical theory and practice, chiefly from the Neyman-Pearson point of view. The references listed in the book provide a very helpful guide to further reading and to original papers.

As might be expected from this author, the book is (with a few exceptions) written most carefully and lucidly, and with an emphasis on exact definition, though difficult proofs are omitted. The book also usefully explains some of the practical methods of analysing genetic data (especially in human genetics).

Professor Elandt-Johnson points out from time to time some of the snags and qualifications, and notes that the conclusions only follow when the original assumptions are valid. However, these necessary disclaimers are not always very prominent. One wonders what a reader new to the subject will make of the (perfectly correct) qualification that the theory of confidence intervals does not enable one to draw any conclusions from any particular sample. In his investigation he will collect many samples, and will want to draw conclusions from them; a qualification of this kind must either seem quite baffling, unless its motivation is explained carefully, or it will simply be ignored.

Again, Professor Elandt-Johnson does not point out the very different reliability of the various methods. In theory, the Hardy-Weinberg law should scarcely ever hold in real populations, since there are always disturbing factors. In practice, it almost always holds, with sufficient accuracy for any practical purpose. In contrast, the elegant theory of ascertainment probability for a rare genetic condition must be scarcely ever applicable to real data. For it is based on an assumption that all affected individuals have, independently of one another, the same probability of being a proband (that is, of coming directly to the notice of the investigator, excluding cases found only because they are relatives of some other affected individual). It is very difficult to think of a reasonable and practicable method of sampling with the property that two affected brothers have independent chances of being probands in this sense. (Random sampling is not practicable here.) For example, one commonly used sampling procedure will be through enquiries made to medical practitioners; but brothers, especially if they are young, will often have the same physician. Moreover, failure of this assumption will quite appreciably affect the accuracy of the conclusions obtained. The perfection of the book, in which the subject is mostly presented neatly and tidily in best Sunday dress, also conceals the fact that real life is not always so perfect; populations are heterogeneous, genetic conditions do not always follow Mendelian ratios, estimates of mutation rates are inconsistent, samples are heavily biased, and major theoretical problems remain unsolved or controversial. For these reasons the book must be read with caution and with awareness of reservations. Subject to this, it represents a useful exposition of some of the most important parts of mathematical genetics.

CEDRIC A. B. SMITH

Liquid Scintillation

Liquid Scintillation Counting. Edited by A. Dyer. (Symposium at University of Salford, September 1970.) Pp. vii+133. (Heyden: London, New York and Rheiner, July 1971.) £4.60; $12.

THE principle of liquid scintillation counting is deceptively simple. Its practice has become remarkably complex. A specimen labelled with a β-emitter, usually tritium or carbon-14, is introduced into a fluorescent organic solution, and the scintillations induced in the solution by the β-particles are detected by a pair of photomultipliers, operating in coincidence to minimize background noise. With the development in recent years of many increasingly sophisticated automatic counting instruments, liquid scintillation counting has become established as the basic technique for the radio-assay of biological specimens.

The complexities arise from the variety of biological materials and their physico-chemical properties; the numerous sample preparation techniques and solubilizers which are used to incorporate them into the solution; the many different scintillator solutions which are used, and the intricate sequence of events which constitutes the scintillation process. To quote Dr Kalbhen's concluding remarks at this symposium: "For each variation in solvent, solute and sample preparation techniques, it is necessary to recalibrate the liquid scintillation counter to optimal counting conditions. It has become quite impossible to compare quantitatively counting results from one laboratory with those from another". In spite of these limitations, which may ultimately be overcome by the adoption of standardized sample preparation methods which convert all biological materials into the same combustion products, satisfactory liquid scintillation counting methods have been developed for the routine radio-assay of a very wide range of biological materials.

The thirteen papers in this slim volume were originally presented at a two-day symposium at the University of Salford. Topics discussed include chemiluminescence as a problem and as an analytical tool, the emission spectra of liquid scintillators, the determination of the activities of carbon-14 and electron-captive nuclides, and a new gelifying agent for specimen incorporation. Three papers are devoted to the use of computer techniques for data processing and quench correction, and two deal with specific biological applications to thyroid cell DNA, enzymes and drug actions. Two papers on scintillations in liquid helium and the design of a liquid helium neutron polarimeter seem strangely out of context. The contents of the volume seem to be too diverse to appeal to anyone who is not already a specialist in the subject. J. B. BIRKS

Nuclear Reactions

Nuclear Reactions and Nuclear Structure. By P. E. Hodgson. Pp. xii+661. (Clarendon: Oxford; Oxford University: London, October 1971.) £14.50.

PETER HODGSON is a physicist's physicist, a man poised half way between the theoretical and experimental world, who provides the necessary bridge between the desk bound and bench bound nuclear physicist. Although truly a theoretician, Hodgson still hankers after his experimental beginnings as a research worker and with such a background he is well suited to write a book such as this that aims particularly at the experimental physicist. It is this background that perhaps makes this book the eminently readable book that it is—a rare quality in a volume that is a comprehensive survey of a kinetic subject such as nuclear reaction theory.

Nuclear Reactions and Nuclear Structure comes eight years after the author's first book in this field, *The Optical Model of Elastic Scattering*, also published by the Clarendon Press. Not unnaturally there is a deal of common ground covered but these sections have been completely revised with references included up to 1971. In 1963, Hodgson treated only the scattering of nucleons but now he turns his attention to the full complexities of nuclear reactions as well without, however, going into details of how gamma ray data can aid in unravelling the details of reaction mechanisms. He says in the introduction that the subject matter covered is a matter of his own taste and interest. It is thus not surprising that in this book we find a most comprehensive and up to date treatment of the optical model and distorted wave treatment of nuclear reactions. It is unfortunate in a way, but certainly not so in another, that such a book as this gets dated very quickly, and one has only to compare *The Optical Model of Elastic Scattering* and the present volume to realize how fashion has changed in the field of elastic scattering in the past eight years.

What sets Hodgson's book apart is his frequent comparisons between experiment and theory, exemplified by figures taken from published articles. This will be welcomed by the experimental nuclear physicists who often have to suffer books that make no attempt to marry theory and experiment. Hodgson also makes no attempt to involve the reader in mathematical calculations and, as he rightly points out in the introduction, the techniques of mathematical manipulation spread over several chapters would be indigestible to the reader. The experimenter, of course, is more concerned with the implications of how the theoretical calculation fits his results than with the subtleties of Racah algebra.

There is no doubt that all experimental physicists working in the field of nuclear reactions should have, and indeed will want, a copy of this book. It is unfortunate that the price will make it improbable that they can. It is a sign of the times that whereas *The Optical Model of Elastic Scattering* cost £1.50 for 211 pages, the present book costs £14.50 for 661 pages, a somewhat disproportionate increase.

ALUN JONES

Fossil Mammals

Early Mammals. Edited by D. M. Kermack and K. A. Kermack. (Supplement to the *Zoological Journal of the Linnean Society.*) (V.50.) Pp. xiv +203. (Academic: New York and London, September 1971.) £5.30; $15.50.

The Age of Mammals. By Bjorn Kurten. Pp. 250. (Weidenfeld and Nicolson: London, October 1971.) £3.50.

Mammals had already passed through two-thirds of their evolutionary history before the so called Age of Mammals began, but knowledge of the Mesozoic mammals is very scanty. In recent years, however, there has been a considerable revival of interest, stimulated by the discovery of new material, and the study of Mesozoic mammals is now one of the main growing-points of vertebrate palaeontology. *Early Mammals* is a collection of papers given at a symposium arranged by the Linnean Society in June 1970. It provides an excellent survey of the state of knowledge at that date, and should be useful to students as well as to research workers.

In view of the nature of the fossil material it is natural that most of the papers are concerned with teeth and jaws. J. A. Hopson describes the replacement of the teeth in the cynodont *Diademodon* and discusses the origin of the mammalian system of tooth-replacement; R. G. Every and W. G. Kühne interpret wear-facets on teeth in terms of "thegosis", a mechanism of sharpening the cutting edges; A. W. Crompton interprets the same facets in terms of occlusal relations, in a well illustrated discussion of the origin of the tribosphenic molar. Other papers describe new material, again consisting of jaws and teeth: J. R. E. Mills on the teeth of *Morganucodon,* B. Krebs on dryolestid mandibles from Portugal, W. A. Clemens and P. M. Lees on Early Cretaceous mammals from England, B. H. Slaughter on Albian mammals from Texas and R. C. Fox on Campanian mammals from Alberta. Only one paper deals with any aspect of skull structure: this is by K. A. Kermack and Z. Kielan-Jaworowska, who compare the brain cases of recently discovered Mongolian Cretaceous multituberculates with those of *Morganucodon* and the present-day monotremes. It is a pity that it was not possible to include at least a preliminary description of the skull and skeleton of *Morganucodon,* which have been under study for some years. In an interesting paper W. A. Clemens speculates on ecological and zoogeographical aspects of mammalian evolution in the Cretaceous, including the yet unsolved problem of how marsupials got into Australia. Finally, G. G. Simpson, whose monographs of 1928–29 form the foundation of all subsequent work on Mesozoic mammals, gives a valuable critical survey of this developing field.

Only when we reach the Cainozoic does it become possible with some degree of confidence to visualize the mammals as living animals. In *The Age of Mammals* this is what Dr Kurten has set out to do. Writing in a very readable style, and avoiding technical terms as far as possible, he deals in turn with each epoch, describing the geography, climate and vegetation, together with the principal deposits in which fossil mammals occur. Stratigraphical correlation tables and palaeogeographical maps are provided. Against this background the mammals are described in sufficient detail to fit them into their environment. The reader is given a vivid impression of the successive phases of mammalian evolution during the past sixty-five million years, and an indication of the nature of the evidence on which the story is based. Some of the more interesting birds and reptiles are also treated. The book is well illustrated by sixty-seven line drawings and eleven plates by Margaret Lambert depicting life reconstructions of a wide range of fossil forms.

The *Age of Mammals* is not a textbook but an imaginative synthesis which should provide valuable background reading for students of zoogeography and mammalogy as well as vertebrate palaeontology. As a synthesis it also has interest for the specialist, though inevitably he would disagree with some of the details. There are occasions when the author allows his imagination to run rather far from the evidence: because the teeth of *Planetotherium* resemble those of the modern colugo it does not follow that it was a glider. The list of references is rather short, and there are several instances where one is left to guess at the source of information. While applauding the attempt to avoid technical terms, the use of unfamiliar English names for fossil groups sometimes leads to obscurity: for example, the term "thunderbird" is introduced on p. 171, but not till p. 183 is it revealed that the author means the Phorushacidae. Another minor criticism is that the palaeogeographical maps do not always agree in detail with the descriptions in the text.

Nevertheless, Dr Kurten has succeeded in making the fossils live again. The book is full of vivid images: we can see herds of palaeotheres visiting their selected water-holes, a pantodont defending itself with its heavy paws, a mammoth using its curved tusks to scrape the snow off grass. Whether these things really happened we do not know, but we do know that fossils were once living animals. Anyone who thinks that palaeontology is a dull, mind-narrowing subject ought to read this book.

P. M. Butler

Anti-antibodies

Human Anti-human Gamma-Globulins: Their Specificity and Function. (Proceedings held in Lund, October 1969.) Edited by R. Grubb and G. Samuelsson. Pp. xii+227. (Pergamon: Oxford, September 1971.) £6.00.

In recent years, immunologists and geneticists have come to rely heavily on the properties of anti-antibodies. Studies of inheritance of genetic markers of immunoglobulin molecules, synthesis of these proteins at cellular level and the phenomenon of allotype suppression induced in rabbits and mice treated during foetal or perinatal life are all based on the use of anti-antibodies. This book, however, contains only a few papers dealing with these topics; the chief concern of the symposium held in Lund was the discussion of the origin, function and effect of anti-antibodies. Whether this aim was achieved during the meeting, and also whether the participants found the discussion informative, is difficult to say. In my view, however, the published proceedings fail to provide the reader with much valuable information. One reason is that the majority of the papers published in the book are "in abstract form only, as most of the work is already in the process of publication elsewhere". This means that out of the five papers included in session 5 dealing with the presence of immunoglobulin molecules on the surface of lymphocytes, three are no more than two pages long and the results have already been published *in extenso* in scientific journals. One of the few long papers published in the book also appeared recently in an immunological journal.

I was particularly disappointed to notice that the special lecture under the intriguing title of "Foetomaternal histocompatibility in toxaemia of pregnancy" was summarized in three and a half pages, of which three tables and a figure comprised a major portion. Finally, the English of some of the papers is rather poor and the meaning occasionally obscure. It should also be mentioned that the title of the book is rather misleading, since many papers discuss the function and the properties of anti-antibodies which are neither of human origin nor directed against human γ-globulin.

The book, of course, contains some original and informative data; particularly interesting is the work of Speiser and collaborators on the transient nature of anti-Gm which appears during childhood.

M. Adinolfi

CORRESPONDENCE

Alice Economics

SIR,—We feel that you have failed to understand the issues involved in continued economic growth (*Nature*, **234**, 2; 1971). It is undeniable that pollution has accompanied economic growth. It may be that economic resources are required to stem the effects on the environment, but before this can be brought about a whole new political atmosphere is needed: our economic efforts must be redirected. Much of the economic effort in modern industrialized communities, such as the EEC, is invested in the production of non-essential consumer goods, aerospace and defence technologies, and other areas where raw materials are consumed almost unthinkingly and where attendant pollution problems are solved, if at all, only as an after-thought.

The industry of the future should be one in which a much greater proportion of the materials used will already have been recycled many times. It should be manufacturing items which are more directly applicable to the world's problems, such as medical goods, birth control devices, agricultural materials, and housing materials. The need for these goods is mainly in poorer countries. The required revolution in the foreign aid and internal economic policies of the rich countries will not be achieved without a radical change in political atmosphere, and we share Professor Scorer's disappointment that no mention of these points was made in the EEC debates.

It is indeed no accident that the richest nation is the most worried about pollution, since it has considerably more than the rest of us, as a result of greater economic advance, and is feeling the effects earlier than most. In pollution terms, and in terms of *per capita* use of natural resources, one American has a far greater impact than, for example, one Indian. Also, many American citizens are aware of the continuing failure of their political leadership to deal with these problems, and do not share your blind faith that all will turn out right in the end.

What you ignore is that we live in a world which has only a limited quantity of raw materials and can only support a finite population. The plain fact is that the world could not support even its present population if everyone shared the American standard of living: if we wish everyone to be decently fed and housed, somebody has to be prepared to give. That includes us.

Yours faithfully,

C. J. BOLTON
J. E. CORDWELL

154 Redland Road,
Bristol BS6 6TD

Alice Economics

SIR,—I find the editorial attitude expressed in Professor Scorer's letter to *The Times* distressing; and, worse, bigoted. If he is irresponsible in his "environmentalist" attitudes, so indeed are you with your "growth is a prerequisite to improvement" attitude. Do you have a connexion with economists? It appears to me that only they of our ideological dinosaurs continue to put all their eggs in the long since worn out basket of required economic growth via an expanding population. Surely economic growth can also be achieved with a static or even a decreasing population?

Overall there is perhaps only one obvious fact, one which you choose to ignore, and which is the basis of Professor Scorer's letter. This is the need for a fundamental change of some sort. To a mathematician, or indeed any logically inclined person, the exponential curve of population growth can have only one answer, and that is change. The change may be controlled or cataclysmic, but change there will be.

Your comparison of our small and already overcrowded island with the USA (some four times the population in around forty times the area) is ridiculous. That country, with present-day technology, is already capable of feeding its estimated population for the year 2000 and beyond, while our population has already outgrown our own food supply. Indeed, even India, with around eight times the population in twelve times the area, is better placed; when the pressures arise, we shall be among the first to experience them.

Your dismissal of the pollution problem on the grounds of lack of specificity is irresponsible. More worrying is your lack of awareness that the decrease in fish landings to which you refer is itself a form of pollution. Pollution by taking needs to be considered with pollution by dumping. The Kansas dust-bowls were not produced by the dumping of dust.

Your patronizing attitude to our poorer neighbours must irk them in the extreme. Must they continually rely on aid based on a fraction of our growth? Again a mathematically (and historically) unacceptable model in the long term.

May I say finally that I already find the pressures of today's society bearable only with difficulty, and that I take Professor Scorer's ideas seriously enough to wonder if I wish to take part in your rich and sterile utopia with its increasingly (and necessarily) controlled overpopulation.

Yours faithfully,

I. A. ELLIS

Westfield College,
University of London,
London NW3

Ethics for Authors

SIR,—As editors of a monograph series published by a well known university press, we have each had recently the following experience. A competent scientist asks us to consider publishing a book which he has on hand. We reply showing interest, and negotiations begin, involving the assessment of a synopsis and sample chapters, a check on the existing literature, and advice to the press to publish. Improvements of style and content are suggested to the author, and a formal contract is prepared. This is a lengthy procedure and may take many months. We are then told that the finished book has been accepted by another publisher, with whom, in fact, the author was simultaneously negotiating.

In the selling of a house such conduct is usually regarded as dishonourable, if not quite actionable. In the jungle of commercial publishing one must, no doubt, be prepared for such dishonesty. But in the production of specialized scholarly works this is unethical behaviour, not at all in the interests of authors themselves.

It is true that we are paid as editors in proportion to the success of the books that we get into print. Some unscrupulous editors and publishers make a quick profit by accepting every manuscript, without question or revision and wax rich on high-priced sales to libraries. But most scholarly editors do not do this sort of job solely for monetary gain: they regard their labour as a general service to the scholarly community, to maintain high literary and scientific standards, for the benefit of their colleagues as authors and as readers.

Our complaint is at the selfish and frivolous waste of our professional time and effort in the name of "free competition". Not nearly enough trouble is taken by most scientists to improve the quality of the books they must read: it is scandalous that the little we do should be spent thus fruitlessly. It is poor consolation, incidentally, to observe afterwards that the author has not hesitated to benefit (without acknowledgment) by the improvements we have proposed.

We also believe that the credibility of scientific publications depends upon an agreed and orderly framework, in which well qualified editors and reputable publishers respect themselves and one another. The margins of technical book publishing are not so elastic as to allow wide variations in the real terms that can be offered to authors. The ultimate financial return on a book depends on much more imponderable factors than the apparent royalty percentage or the quality of the burgundy at a tax deductible lunch. A good book can easily be published and an author does much better by bargaining hard and honestly with almost any single good publishing house than by "shopping around".

Some people do not seem to have thought this out, and fall for the fast buck. Let us spell it out to them. They know well enough that they must not submit the same research paper simultaneously to two different journals. We suggest that the behaviour here reported must be considered a comparable breach of the unwritten ethical code of the scientific community.

Yours faithfully,

M. M. Woolfson
J. M. Žiman

H. H. Wills Physics Laboratory,
Royal Fort,
Tyndall Avenue,
Bristol BS8 1TL

Viral DNA Integration

Sir,—In a review article "Vintage Year for Tumour Virology" (*Nature*, **233**, 28; 1971) John Tooze states: "and the recent experiments of Wall and Darnell (*Nature New Biology*, **232**, 73; 1971) dispel any doubts about the integration of polyoma (actually SV 40) virus DNA into host cell DNA". Recent experimental evidence throws new light on this situation (Gelb *et al.*, *J. Mol. Biol.*, **57**, 219; 1971). Because of it, there is to my knowledge no published evidence which conclusively demonstrates the integration of SV 40 DNA into the DNA of the transformed host cell. Gelb *et al.* have recently shown that host specific SV 40-like sequences exist in non-transformed cell green monkey and mouse DNAs. About one-half copy of host specific SV 40-like sequence is present in each cell. Published experiments designed to demonstrate the integration of SV 40 into transformed cell DNA have relied on the reaction of SV 40 C-RNA (RNA made *in vitro* from SV 40 DNA) with transformed cell DNA which had a molecular weight much higher than SV 40 DNA (Sambrook *et al.*, *Proc. US Nat. Acad. Sci.*, **60**, 1288; 1968). It was assumed that any reaction of C-RNA was with virus specific SV 40 sequences, which had been integrated into the host cell DNA. However, the existence of host specific SV 40-like sequences in DNA from transformed cells complicates the interpretation of these data. It is not known whether the C-RNA reacted with host or virus specific SV 40-like sequences. The interpretation of Sambrook *et al.*, that SV 40 DNA is integrated, rests entirely on the greater degree of reaction of SV 40 C-RNA with high molecular weight SV 3T3 cell DNA than with PY 3T3 high molecular weight DNA. This result could be the consequence of: (*a*) the integration of virus specific SV 40 sequences in the host DNA, or (*b*) the differential replication in SV 3T3 cells (and not in PY 3T3 cells) of the chromosomes which contain the host specific SV 40-like sequences.

The data of Lindberg and Darnell (*Proc. US Nat. Acad. Sci.*, **65**, 1089; 1971) and Wall and Darnell are also difficult to interpret for the same reason. It is not known whether the large RNAs they detect, which contain both SV 40-like and host specific sequences, arose from virus specific SV 40 sequences or from the host specific SV 40-like sequences which are present in non-transformed cells.

In summary, I do not believe that the virus DNA integration into transformed cell DNA has been proven.

Yours faithfully,

David E. Kohne

Biophysics Section,
Department of Terrestrial Magnetism,
Carnegie Institution of Washington,
Washington DC 20015

Library Optimum

Sir,—In his recent article[1] B. C. Brookes propounds an ingenious mathematical framework to determine which periodical volumes a library should hold. He is careful to point out that the selection will need regular review and revision, in case the value of the ageing factor *a* or the contents of the Bradford set change from year to year. There is as yet very little experimental evidence on the consistency of either. Such limited evidence as there is suggests that the ageing factor is reasonably constant. But the position of the Bradford set is less satisfactory. The Nature Conservancy librarians (J. M. Weingott and S. M. Penny, unpublished) have lent me a list of titles cited in the *Journal of Ecology* three or more times in 1955–56, and a similar list for 1965–66. There are 150 periodical titles in the two lists, but only forty-two (28%) appear in both. Of the thirty-three titles cited nine or more times in either year, only eight (25%) attained that level in both, and twelve were cited less than three times in the other year. The Kendall rank correlation coefficient between the two years is 0.18 and not significant.

There is another major practical problem. The article assumes that the data analysed to obtain ageing or utility factors and Bradford sets are valid parameters of the relative value of the literature to the readers. There is no mention of the type of data to use. The reader who sought guidance from the earlier literature cited would find practical techniques described in which analyses of citation frequencies are used to calculate *utilities* discussed in terms of library use. Krauze and Hillinger[2] have discussed the difference between citations in one article and future citations to that article. Their work implies a more complex relation between *a* and *u* than Brookes suggests. In any case, the validity of citations for forecasting library consultations remains unproven, and there are *prima facie* reasons why the relationship is not necessarily close. For example, one item in a list of references is often intended to lead to a chain of earlier papers. Again, each citation represents an author's selection from a wider group most of which he has consulted in a library. In neither case is there any inherent reason for similarity of age distribution or of pool of titles between the list of citations and the items read by the author or his readers.

Most of the practical studies of citations or library use have so far been based on the relation between frequencies and age or title, without considering the number of items available for reference. But, to be useful as parameters of the relative value to scientists of groups of volumes, the data must be presented as the number of references per available item, and not as the numbers from groups of differing size. The need to correct "obsolescence rates" for the fact that there is much less of the older literature to cite or read is becoming generally recognized. When the appropriate corrections are made, it has been shown[3] that in some library contexts the older literature can be more heavily used than the younger. In all calculations based on Brookes's utility concept it is therefore essential that the utility factor *u* be derived from an ageing factor *a* representing the change in references-per-item (not the crude changes in references) with age. The terms item-consultation decay rates and item-citation decay rates have been suggested[3] for suitably corrected factors.

Similar considerations apply equally to the data for obtaining a Bradford set. One citation in 1970 to a periodical first published in 1965 is much more significant than to one first published in 1960 because there are twice as many volumes of the latter available to be cited. Applying a correction to the Bradford sets in the *Journal of Ecology*, to allow both for the age of the periodical title and for an item-citation decay rate of 0.95 (a preliminary value obtained from citations in the same journal), raised the Kendall rank correlation coefficient to 0.25: but this is still not high enough to place much reliance on the predictive value of a Bradford set for ecological literature.

Scientists and librarians would therefore be wise to approach an optimum $P\%$ library with caution and to check that the data they use for measuring the relative value of parts of their stock are suitable for the purpose and consistent from one occasion to another. Until they have done so they should not take any irrevocable decisions on the basis of Bradford sets or ageing factors.

Yours faithfully,

A. Sandison

National Reference Library of
Science and Invention,
Holborn Division,
25 Southampton Buildings,
London WC2A 1AW

[1] Brookes, B. C., *Nature*, **232**, 458 (1971).

[2] Krauze, Tadeusz K., and Hillinger, Claude, *J. Amer. Soc. Inf. Sci.*, **22**, 333 (1971).

[3] Sandison, A., *J. Doc.*, 27, 197 and 189 (1971).

Sex Discrimination

Sir,—We were startled to read in your issue of October 29 (*Nature*, **233**, xxii; 1971) an advertisement, placed by the Australian Atomic Energy Commission, describing a research post and ending with the statement "Female rates slightly less than male rate quoted". The fact that sex discrimination is still an official policy of the Australian government does not, in our opinion, absolve a private journal such as yours from the responsibility not to abet discrimination based on race, national origin, political or religious belief, or sex. We presume, for example, that *Nature* would not now accept advertisements that were discriminatory with respect to colour or religion. We look forward to a prompt and public statement by *Nature* of a new nondiscriminatory advertising code.

Yours faithfully,

David Layzer
Randy Levine
Martha E. Schwink
H. T. Doyle
Joseph H. Schwarz
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Jean H. Goad
Kurt S. Anderson
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Sandra M. Faber
Suzanne McKee
Christopher J. McKee
David E. Harris
Charles King

Robert Noyes

Harvard College Observatory,
Cambridge,
Massachusetts 02138

Obituary

Dr Colin Cadman

Colin Houghton Cadman, plant pathologist and Director of the Scottish Horticultural Research Institute, Dundee, died on September 27, aged 55.

After graduating from Liverpool University with First Class Honours in Botany he first worked at the Scottish Plant Breeding Station, Edinburgh, on the genetic control of the reaction of potato plants to virus infection. This work, which formed the basis of his PhD thesis, was the origin of his interest in plant viruses, and he devoted the rest of his productive research career to their study.

In 1943 the Scottish Raspberry Investigation, directed from East Malling Research Station, was set up at Dundee and Cadman became its resident pathologist. The main aim of this unit was to tackle the problems posed by the degeneration diseases of the raspberry, a crop more intensively grown in the area than anywhere else in the world. During the next eight years, by shrewd observation and simple experiments, he differentiated and identified many new viruses affecting raspberry and showed that some were spread by aphids. He began to propagate healthy stocks and became the foremost expert in raspberry viruses.

When the Scottish Horticultural Research Institute was founded in 1951, he became the head of its Plant Pathology Department and his research entered its most imaginative period. He discovered that a virus could be transmitted experimentally to herbaceous test plants by inoculating them with sap from raspberry plants affected by the important leaf curl disease. This led to the recognition of a group of viruses which cause ringspot symptoms in plants, have wide host ranges including numerous weed and crop species in many countries, and which spread through the soil. Following the American report that grapevine fanleaf virus has a nematode vector he showed that arabis mosaic virus, one of the soil-borne ringspot viruses found in Britain, is similarly transmitted; and that grapevine fanleaf virus can be sap-transmitted to herbaceous test plants and is serologically related to arabis mosaic virus. Other kinds of nematode-transmitted viruses were also found and one, tobacco rattle virus, was consistently obtained from potato tubers affected by spraign, a common disease that had previously defied efforts to determine its cause. A new field of plant virology was opened up and Cadman's laboratory became a centre of international repute for the study of soil-borne viruses.

He also did other pioneering work. He showed how to avoid the effects of substances that hindered the detection of viruses in woody species; he found a virus that was spread between raspberry plants, not by vectors but in pollen; and, independently of German workers, he showed that some isolates of tobacco rattle virus existed in plants as ribonucleic acid that was not protected by a protein coat.

His research having been the main foundation of the scientific reputation of the Scottish Horticultural Research Institute, he became its second Director in 1965. During the next six years he achieved a transformation. Research was reorganized to stimulate scientific productivity, and a comprehensive building programme started to provide improved accommodation and modern facilities. He fostered closer links with the farming and processing industries, he set up the Institute Association to bring the two together and keep them informed of research results, and he did much to launch the Scottish Nuclear Stock Association, which was founded initially to propagate the Institute's virus-free raspberry stocks for distribution to growers.

Colin Cadman had a quiet, sympathetic and perceptive but determined nature, and never took his decisions without careful thought. He gave much unselfish help to younger colleagues, and encouraged them to pursue problems in depth regardless of whether immediate practical applications were likely to result. In private life he was a good field botanist who loved the Scottish hills and was an accomplished cellist. He was not married but will be much missed by many friends.

Announcements

University News

Dr Alan Thompson, University of Edinburgh, has been appointed to the new chair of economics of government in **Heriot-Watt University.**

Dr M. H. Day has been appointed to the chair of anatomy tenable at St Thomas's Hospital Medical School and **Dr C. D. Marsden** has been appointed to the chair of neurology tenable at the Institute of Psychiatry and King's College Hospital Medical School, **University of London.**

Professor Richard Lynn has been appointed to the chair of psychology at the **New University of Ulster.**

Appointments

Lord Orr-Ewing has been appointed deputy chairman of the **Metrication Board.**

Errata

THE title of the article by V. P. Starr (*Nature*, **233**, 186; 1971) should be "Eddy Viscosity and the Solar Rotation".

IN the article "Cyclic Expression of Blood Group Determinants in Murine Cells and their Relationship to Growth Control" by D. B. Thomas (*Nature*, **233**, 317; 1971), the abscissa to Fig. 2 should read: "Hours after release of double thymidine block".

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

The Science of Botany: From Simple Lore to Social Need. By Professor A. G. Morton. (Inaugural Lecture, 15th March 1971.) Pp. 18. (London: Chelsea College, University of London, 1971.) [168

Annual Report of the Meteorological Office 1970. Pp. xii+102. (London: HMSO, 1971.) 80p net. [168

Department of the Environment. Water Pollution Research 1970: The Report of the Water Pollution Research Laboratory Steering Committee with the Report of the Director of Water Pollution Research. Pp. vii+185. (London: HMSO, 1971.) £1.15 net. [178

Department of Education and Science. On Course Bulletin No. 1: Certificate in Office Studies. Pp. 8. (London: Department of Education and Science, 1971.) [178

County Councils Association; Association of Municipal Corporations; Urban District Councils Association; Association of Public Analysts. Joint Survey of Pesticide Residues in Foodstuffs sold in England and Wales, 1st August, 1967–31st July, 1968 (second year). Pp. 38. (London: Association of Public Analysts, 1971.) £1.10 (including postage). [188

Oundle School Natural History Society. Annual Report 1970. Pp. 55. (Oundle, Peterborough: Oundle School, 1971.) [188

Foreign and Commonwealth Office—Overseas Development Administration. Directorate of Overseas Surveys Annual Report for the year ended 31st March 1970. Pp. 69+8 photographs+9 maps. (London: HMSO, 1971.) £1.20 net. [188

Ministry of Agriculture, Fisheries and Food. Technical Bulletin No. 24: The Significance of Winter Rainfall Over Farmland in England and Wales. Pp. vii+69. (London: HMSO, 1971.) 45p net. [208

Central Statistical Office. Statistical News No. 14: Developments in British Official Statistics. Pp. v+26. (London: HMSO, 1971.) 30p net. [208

Other Countries

Pharmaceutical Manufacturers Association Foundation, Inc. 1970 Annual Report. Pp. 30. (Washington, DC: Pharmaceutical Manufacturers Association Foundation, Inc., 1971.) [98

Bulletin of the American Museum of Natural History, Vol. 144, Article 5: A Review of the Pre-Pliocene Penguins of New Zealand. By George Gaylord Simpson. Pp. 319–378. (New York: American Museum of Natural History, 1971.) $2.50. [98

Mutation Breeding for Disease Resistance. (Proceedings of a Panel on Mutation Breeding for Disease Resistance organized by the Joint FAO/IAEA Division of Atomic Energy in Food and Agriculture and the FAO Plant Production and Protection Division and held in Vienna, 12–16 October 1970. Panel Proceedings Series.) Pp. 249. (Vienna: International Atomic Energy Agency; London: HMSO, 1971.) 155 schillings; £2.50; $6. [98

Commission on Undergraduate Education in the Biological Sciences. Publication No. 32: Guidelines and Suggested Titles for Library Holdings in Undergraduate Biology. Edited by Joan Creager. Pp. iv+65. (Washington, DC: Commission on Undergraduate Education in the Biological Sciences, 3900 Wisconsin Avenue, NW, 1971.) *gratis.* [98

The Year Book of the International Council of Scientific Unions 1971. Pp. 241. (Rome: ICSU, 1971.) [98

FAO—WHO—OIE. Animal Health Yearbook 1970. Pp. 334. (Rome: FAO; London: HMSO, 1971.) £1.60; $4; FF20. [108

Environmental Physiology: Nutrition, Pollution, Toxicology, Vol. 1, No. 1, 1971. Edited by J. Clausen. Pp. 1–54. Subscription price: D.kr. 148.00 plus postage D.kr. 12.00 ($21.50) payable in advance. Price per issue D.kr. 40.00 ($5.40). (Copenhagen: Munksgaard, 1971.) [118

Smithsonian Contributions to Zoology. No. 63: Bredin-Archbold-Smithsonian Biological Survey of Dominica—The Dermaptera (Earwigs) of Dominica. By Alan Brindle. Pp. 25. $0.40. No. 81: The Entocytherid Ostracods of Mexico and Cuba. By Horton H. Hobbs, Jr. Pp. 55. $0.65. No. 87: Parasitic Copepods of the Family Chondracanthidae from Fishes of Eastern North America. By Ju-shey Ho. Pp. 39. $0.50. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office.) [128

Record of the South Australian Museum, Vol. 16, No. 7: Acarine and other Microfossils from the Maslin Eocene, South Australia. By R. V. Southcott and R. T. Lange. Pp. 21. (Adelaide: South Australian Museum, 1971.) [128

US Department of the Interior: Geological Survey. Water-Supply Paper 2001-A: Ground-Water and Geohydrologic Conditions in Queens County, Long Island, New York. By Julian Soren. Pp. iv+39+2 plates (Washington, DC: Government Printing Office, 1971.) [128

Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Bulletin 174: Geochemistry of Iron, Manganese, Lead, Copper, Zinc, Arsenic, Antimony, Silver, Tin, and Cadmium on the Soils of the Bathurst Area, New Brunswick. By E. W. Presant. Pp. 93. $2. Paper 71–1: Report of Activities. Part B: November 1970 to March 1971. Pp. vi+139. $2. Paper 71–18: Secondary Fields of a Vertical Magnetic Dipole Above a Thin Horizontal Layer of Conductive Overburden. By A. V. Dyck and A. Becker. Pp. v+25. $1.50. (Ottawa: Information Canada, 1971.) [138

Annual Report of the Inter-American Tropical Tuna Commission 1970. Pp. 127. (La Jolla, California: Inter-American Tropical Tuna Commission, 1971.) [138

Organisation for Economic Co-operation and Development. Science, Growth and Society: a New Perspective. Pp. 113. (Paris: OECD, 1971.) 10 francs; 77p; $2.25; 9 Sw. francs; 7 DM. [138

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NATURE Volume 234
DECEMBER 17 1971

Putting Heads in Bags

THE continuing civil disturbance in Northern Ireland is an important counterpoise against the reputation of the United Kingdom for orderly political processes, but most outsiders have in the past few years been willing to acknowledge that the tension between the Protestant and Catholic communities, exacerbated as it is by poverty, is an intractable social problem. This, at least, was the case until the beginning of August this year, when arrangements were made to detain some hundreds of people under emergency regulations which gave those detained no right of access to the courts. It is fair to say that the governments of Northern Ireland and of the United Kingdom have been reluctant to resort to these measures and even their most severe critics will agree that the decision in favour of internment, right or wrong, was a response to growing violence. In retrospect, of course, it may have been a gross miscalculation to have supposed that detention without trial would have solved important problems. The most serious damage to the reputations of the two governments concerned will, however, in the long run be seen to depend not so much on the process of detention as on the gloss which the government of the United Kingdom has managed to put on some of the events accompanying detention as a result of a report by a committee under Sir Edmund Compton "into allegations against the security forces of physical brutality in Northern Ireland arising out of events on the 9th August, 1971" (Cmnd 4823, HMSO, £0.525).

The circumstances which provoked the report, chiefly allegations by prisoners and their relatives of brutal treatment by their captors, are less shocking than the report of the Compton inquiry, which affects a conveniently pedantic definition of brutality and a disturbing ignorance of the damage that may be done to people by some of the devices which its own proceedings established to have been used in Northern Ireland. Many of the allegations against the British army and the police forces of Northern Ireland are familiar from recent accounts of the ill-treatment of prisoners in places such as Greece and North Korea. Broadly speaking, the Compton inquiry has confirmed the statements of newspapers such as the *Sunday Times* earlier this year that prisoners had been subjected to indignities such as having their heads covered with opaque bags except during interrogation and in solitude, being required to stand facing a wall with legs apart for periods of several hours at a time, being subjected to electronic noise while in a crowd together and being fed with bread and water. The report of the Compton inquiry says that "it was the general policy to deprive the men of opportunity to sleep during the early days of the operation".

Other allegations against the army include tales of being forced into helicopter journeys, according to the army so as to persuade on-lookers that prisoners were being moved elsewhere and according to the prisoners as an attempt to frighten them, and the Compton inquiry says in its report that "it is understandable that they should have been frightened by the unknown and should have thought in the absence of any other reasons that the intention must be to victimize them by putting them through a meaningless exercise involving physical hurt or the threat of it. . . . They seem to have suffered no physical damage but we think the physical experience they were forced to go through under these circumstances does constitute a measure of ill-treatment." Elsewhere, at a military prison at Ballykinler Camp, prisoners were required to perform painful physical exercises for long periods of time and the Compton inquiry says "We think it is plain that these compulsory exercises must have caused hardship to some at least of those who were made to do them, especially those in poor physical condition. . . . On the other hand we do not regard the exercises as cruel, if the adjective means that the exercises were thought of and carried out with a view to hurting or degrading the men who had to do them. We prefer to take the view that the exercises were devised to counteract the cold and the stiffness of which the arrested persons complained, but that it should have been foreseen that a system of voluntary changes of position at set times was bound to turn into a form of physical drill compulsorily performed without regard to the relative capacity of the performers, and that the routine was thoughtlessly prolonged after it had served its proper purpose. We think there was lack of judgment here, but not cruelty or brutality, and we think the complainants may have suffered hardship but we made no findings of deliberate ill-treatment."

To its credit, the commission does publish in its report detailed accounts of how individual prisoners were treated and ill-treated. The commission says that it was probably wrong to have discharged Mr Elisha Anderson, at fifty-five and with a chronic heart condition, barefoot into a road strewn with rubble, that Mr Gerard Campbell, whose wrists had been tied and head covered with a sandbag, was so dealt with because of an order which "showed lack of judgment", that Mr William Gilmore was injured by a rubber bullet fired without cause, that Mr Joseph Hughes was held in what is called the "Kado" grip, the effect of which "can be harsh, but it is a recognized method for the controlled use of force", and that Mr J. Moore was roughly and wrongly arrested. In short, the inquiry provides a wealth of evidence to show that the army dealt roughly with its prisoners on August 9 this year. The question is whether the army was brutal.

The Compton inquiry's argument on this point is indefensible. The committee says that having been asked to deal with allegations of physical brutality, "we have confined our investigation to that part of the complaint that relates to physical treatment". The committee goes on to say that brutality is an "inhuman or savage form of cruelty and that cruelty implies a disposition to inflict suffering coupled with indifference to or pleasure in the victim's pain". In all the particular cases listed in the report of the inquiry, it is held that these criteria are not satisfied. Instead, the argument goes, the way in which the prisoners were dealt with constituted not "brutality" but "ill-treatment". In passing, of course, it will be remarked that this is largely a semantic point. In dealing with allegations against an army or a police force, it is plainly unreasonable to ask whether the person carrying out orders to deal roughly with a prisoner has a "disposition to inflict suffering" and it is entirely conceivable that he may execute these orders with such reluctance that he is neither indifferent to his victim's condition nor moved to pleasure by it. In short, the definition of brutality which the Compton inquiry chose to use is one almost certain to ensure that it could not be applicable to the allegations which had been made in Ulster. If this was its starting point, the commission might have saved itself and its witnesses the trouble of having gone to Belfast.

The more serious point of pedantry, however, is the commission's sharp distinction between physical ill-treatment, brutal or otherwise, and other forms of ill-treatment, presumably psychological. It is not necessary to invoke Freud to know that the distinction is unreasonable and untenable. The experience of recent wars has shown plainly enough that assault on a person's sensory apparatus can cause profound physical disturbance. By now, there is also a substantial amount of carefully controlled psychological experiment to show how harmful may be the effects, psychological and otherwise, of sensory deprivation. Professor Patrick Wall and some of his associates have in the past few days been pointing to the evidence accumulated in the past fifteen years which shows how anxiety can be induced by hooding in a few hours, and how enforced sleeplessness can induce psychotic behaviour. It goes without saying that in circumstances like these, prisoners are highly suggestible and therefore likely to be unreliable witnesses. Would the Compton commission have been as sanguine in its statement of the irrelevance of the psychological consequences of the treatment to which prisoners have been subjected in Ulster if it had known of the similarity between the effects of enforced hooding and the effects of treatment with mescalin and other types of hallucinogenic drug?

It is too soon to know what will be the outcome of this shabby inquiry. The wider investigation now begun under Lord Parker may help to provide a better perspective. The most serious danger in the Compton report is not the immediate risk that it may sanction methods of ill-treatment which are disgusting, but that it will somehow help to sanctify the false belief that it is permissible and even possible to distinguish between physical and psychological brutality. To a nation such as Britain, with a long record of denying the unconscious, this may be a palatable conclusion. It is, however, wrong and it is potentially dangerous not merely for the permanent harm which psychological ill-treatment can do to prisoners but for the damage which may be done to society at large by the casual acceptance of psychological brutality in the maintenance of law and order.

The Faster than Sound Machine

In the marriage of national pride with which the British and French governments have invested £850 million in the development of the Concorde aircraft, it has usually seemed as if all the ardour was French and that the British government would have been glad of any excuse to break its contract. Mr Roy Jenkins, who became Minister of Aviation in the Labour government in 1964, made no secret of his annoyance that those who had negotiated the agreement to develop the aircraft had deliberately omitted provisions to regulate the way in which one party might bow out. Over the years, British governments have first shuddered at the rising cost of development, now four times the first estimate, and have then decided to whistle so as to keep their spirits up by saying that it would be folly to back out of a development project which had already cost a very large sum of money and which, in any case, would give Britain and France in partnership a sense or an illusion of "technological leadership".

This is the spirit in which the British government last week dropped all its reluctance about the Concorde project. First of all, on December 7, the two governments agreed in Paris on what is called a pricing formula to be used in negotiations between the manufacturers and potential purchasers of the aircraft. The formula is a device for saying that the two governments will not seek to recover a contribution towards the money spent on development, at least where the first sales are concerned. At the same time, the two governments let it be known that they would encourage the British Overseas Aircraft Corporation and Air France to place firm orders for Concorde aircraft—an open invitation to the airlines concerned to ask for a subsidy. Indeed, there is even talk of the possibility that airlines purchasing Concorde aircraft may be helped along with operating costs as well as with capital. Yet it remains a simple truth that the airlines are not falling over themselves to order this remarkable aircraft. This is why it is still proper to ask awkward questions about the whole project and to ask whether, even at this late stage, it may yet be wisest to abandon the Concorde.

Technically, of course, there is no cause for complaint. Everybody says that the aircraft performs well and, even if the excited applause of ministers fresh from their first flight is no substitute for hard-headed technical appraisal, it seems now to have been demonstrated that the construction of supersonic passenger transport aircraft is technically feasible. Moreover, Concorde is less of an environmental nuisance than has sometimes been supposed. The engines are noisier than they might be, it is true, but nobody is seriously worried about the effects of exhaust gases on the stratosphere and sonic booms can be diminished by keeping the aircraft over the sea for the faster part of its trajectory. In other words, the Concorde has helped to demonstrate that it can only be a matter of time before supersonic aircraft are in regular airline service, providing passengers with the immense convenience of faster long-distance journeys and providing airlines with profits commensurate with the service they will then be able to provide.

The doubts about the Concorde centre not on the rights and wrongs of supersonic flights as such but on the economics of this particular machine. Will it do the job it is intended to perform at anything like the cost that would make the operation profitable? And will airlines be able at this stage in their history to afford the expensive re-equipment which the arrival of the Concorde would imply? The new machine must necessarily be a great economic hazard for those who buy it. However the initial cost of the aircraft may be reduced by what the governments of Britain and France are pleased to call their "pricing formula", the operating costs will be unpleasantly high simply because the aircraft carries so few passengers—a mere 165 or so. Precisely what the total cost will be is likely to be apparent only when airlines have had experience of how quickly these machines can be turned round at each end of a journey. At least if the Concorde is intended to be operated as a commercial proposition, everything will depend on keeping equipment in the air as continuously as possible, and the discussion which preceded the abandonment of the American SST earlier this year showed that airlines are as bemused as anybody by the difficulties of calculating in advance precisely how these aircraft would be operated.

What this implies is that the decision to bring the Concorde into airline service is a leap into the dark for any operator. Prudent people would assume that the possession of a fleet of supersonic aircraft will mean losses. In other words, there is a serious danger that the only customers for the aircraft will be those whose governments persuade them that it is their patriotic duty to place an order. Although Pan-American World Airways is the best potential outlet for sales among strictly commercial airlines, its recent bout of heart-searching may have given it a greater sense of realism than when it first took out an option. Only time will tell. But if it should turn out that the only potential customers for the Concorde are the two national nationalized airlines, then the best course which the sponsoring governments can pursue will be to swallow their pride and cancel the aircraft. In doing so, they will have to acknowledge, painful though that acknowledgment may be, that there is a world of difference between a successful demonstration of the potential benefits of supersonic flight and the development of a commercially successful method for realizing that goal.

Television Frequencies for Grabs

THE 1970s will be formative years for the pattern of broadcasting in Britain, and already there are several signs of the way the wind is blowing. Since the summer, the British government, true to its election promises, has been waving on the bidders for licences to operate commercial radio broadcasting stations. Although such enterprises may not be as profitable in Britain as they are in the United States, long before the end of the decade, the British Broadcasting Corporation will be but one of the sources of broadcast sound. By 1976, however, the government will also have had to make up its mind about the revision and extension of the BBC's charter. The crucial question is the arrangement to be made for television broadcasting, which is why the government should not respond too quickly to the claim last week by the Independent Television Authority for a second television channel for the commercial companies which at present broadcast commercial television signals. The ITA's case is stronger than out-and-out critics of commercial broadcasting will allow, but it would be wrong to make lasting commitments to commercial companies while the future pattern of television broadcasting is undefined.

Within the present framework of broadcasting in Britain, the ITA has a strong case for a second television channel. In its statement last week, the authority said that it is anxious to provide a better service by providing a wider range of programmes. The argument is that while there is only one commercial television channel, the companies have no option but to try to attract the largest possible audience. Although the commercial network in Britain has done some distinguished broadcasting in its time (since the mid-1950s), most of its programmes are undistinguished. What the Independent Television Authority is now asking, on behalf of the programme companies, is that there should be a second channel so that the companies will be able to compete not merely for the mass audience but for what is sometimes called the minority audience and which is at present the theoretical preserve of BBC-2.

The ITA is right to claim that diversification will come about naturally only if the second channel is made available to the companies already blessed with a franchise to operate the first. Throwing the second channel open to a new group of operating companies would merely create a situation in which two parallel commercial networks were competing for the same mass audience, presumably with programmes devised so as to rival each other in imbecility. The difficulty is that if the programme contractors recognize that a second channel endowed with a smaller audience will be a poor magnet for advertising revenue, its programmes will be impoverished by parsimony. (Too much success might create other difficulties, and might, for example, further undermine the British newspaper industry by siphoning off advertising revenue.) The extent to which the ITA would be able to make the programme contractors toe a more enlightened line is another imponderable—in the past, contracting companies have been able to wriggle off painful hooks by pleading poverty.

The most serious argument against the new proposals is not, however, that they may not work as the ITA now promises but that it is quite absurd that a country such as Britain should at this point commit itself to a pattern of television broadcasting which provides for merely four channels. Why is so little use being made of the 376 MHz of the UHF band given over to television broadcasting in Britain? This substantial slice of the spectrum has been divided into channels each 8 MHz wide, and care has been taken to construct a network of broadcasting masts which provides respectable coverage of most parts of Britain (with the notorious exception of northern Scotland). The intention has been to build a network which can provide the whole country with the same service. What this implies is that if one transmitter is given four channels on which to broadcast two UHF signals for the BBC and two for the commercial television companies, each neighbouring transmitter must be given four entirely different channels so as to avoid radio interference. The result, of course, is that the available band-width is rapidly consumed.

If there is to be a uniform television service for the whole of Britain, there is no doubt that the available band-width is sufficient for only four separate networks of programmes. The question that should be asked, however, is whether it is necessary, let alone desirable, to provide a strictly uniform service. If there are to be minority programmes, might they not most efficiently be centred on the large cities? And might not there be advantages in arrangements which allow, say, 90 per cent of the British population to have access to six choices of broadcast programmes even if the remaining 10 per cent were compelled to put up with fewer than four? As things are, there is certainly no prospect that broadcast television will be able to offer the British public anything like the diversity of programmes which is certain to be commonplace elsewhere by the end of the century.

Another uncertainty in the pattern of broadcasting in the late 1970s is the extent to which the British government will actively encourage the development of cable television. Although some parts of the country, especially in hilly regions where television signals are not easily received, are well provided with cable services, the Ministry of Posts and Telecommunications has not made up its mind about the future of multi-channel cable television. By all accounts, it is waiting for Sir Robert Cockburn's Television Advisory Committee. The difficulty is not merely to know who should be responsible for laying and for financing urban networks of coaxial cables, but also that of deciding who should have access to broadcasting stations linked with them. The ideal is that the maintenance and operation of the cable system should be separated from the right or responsibility to provide programmes. Moreover, there is every reason why the same separation should be made between the technology of television transmission and the provision of programme material. In other words, there is something to be said for putting the BBC on the same footing as the commercial broadcasting companies, for whom the ITA provides central engineering services. Whether one public authority could broadcast television signals and operate coaxial cable networks is a more tricky question. Until that and related problems are answered, however, it is hard to see how any government could make a sensible decision on the future of British broadcasting.

For the British Government, the problems occasioned by the need to provide a more rational basis for broadcasting in Britain touch several parts of the government machine. One important issue to be decided is whether the Post Office should retain its monopoly on the provision of telecommunications links within the country—as things are, even the networking arrangements by means of which the commercial television companies and the BBC transmit from one point to another are owned or at least licensed by the Post Office. There have been circumstances in which television relay companies have been allowed to set up their own arrangements for distributing signals, but it remains to be decided who, if anybody, would be able to operate a network of coaxial cables designed not merely so as to distribute television signals but also the other signals which might profitably accompany ordinary television signals. After all, in due course there is every reason why the same cable network should be used for television transmission and even such urban refinements as burglar alarms and the like. Obviously the separation of such a system from the Post Office would thoroughly undermine the basis on which telecommunications in Britain are at present organized. That would mean too much disruption, but there is no doubt that the Post Office itself is slow to recognize the benefits that could come from a vigorous exploitation of a coaxial cable network for distributing video signals. At least one outcome of the present concern for the reorganization of broadcasting services should be an explicit set of marching orders for the Post Office, which must be made to act more quickly than in the recent past.

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100 Years Ago

NATURE

"University of London, Burlington Gardens, W.,
"December 5th, 1871.

"MY DEAR TYNDALL,—If I correctly apprehended what you said at the Dinner of the Royal Society in regard to Dr. Mayer, you repeated what you had previously stated in your Lecture at the Royal Institution in 1863, as to the entire ignorance of Mayer's work which prevailed in this country until you brought it into notice on that occasion.

"Now, I very distinctly remember that a few days previously to that Lecture, I mentioned to you that as far back as 1851 I had become acquainted, through the late Dr. Baly, with one of Dr. Mayer's earlier publications; and that, in bringing before the readers of the *British and Foreign Medical Review* (of which I was then the Editor) the 'Correlation' doctrine, as developed in Physics by Grove, and in Physiology by myself, I had stated that we had both been to a great extent anticipated by Mayer—as I should have shown much more fully if the pamphlet had earlier come into my hands.

"I also most distinctly remember that, as you stated in that Lecture, no one in this country—'not even Sir Henry Holland, who knows everything'—had ever heard of Mayer, I spoke to you again on the subject a few days afterwards; and that you then expressed your regret at having entirely forgotten what had previously passed between us on the subject.

"As it would seem that this second mention of the matter has also passed from your mind, I shall be obliged by your looking at the passages I have marked in pp. 227 and 237 of the accompanying volume, from which I think that you will be satisfied that I had at that date correctly apprehended Mayer's fundamental idea, and that I have done the best to put it before the public that I could under the circumstances—the article having been in type and ready for press before his pamphlet came into my hands.

"Since, in thus bringing forward Mayer, I spontaneously abdicated the position to which I had previously believed myself entitled, of having been the first to put forward the idea that all the manifestations of Force exhibited by a living organism have their source *ab extra*, and not —as taught by physiologists up to that time—*ab intra*, I venture to hope that you will do me the justice of stating the real facts of the case in a short communication either to the *Athenæum* or to NATURE.—I remain, my dear Tyndall, yours faithfully, "WILLIAM B. CARPENTER

"Prof. Tyndall."

From Nature, **5**, 143, *December* 21, 1871

OLD WORLD

ESRO

Italians Frustrated

IN spite of all the entreaties of recent weeks and a last ditch offer by the Italian government, Esro decided last week that it would stop supporting the present scientific activities at the European Space Research Institute (Esrin) at Frascati, Italy, after September 1973. The door is not completely closed, however, and as a sop to the scientists and others that have been fighting hard to keep Esrin as a viable scientific entity the Esro council suggests that "additional Esro activities appropriate to location at Frascati are to be investigated in cooperation with the Italian authorities".

It now remains to be seen whether the Italians carry out their threat (see *Nature*, **234**, 3 ; 1971) to withdraw from Esro as their plan for an Esro/Centro Nazionale delle Richerche (CNR) collaboration has not been accepted by the council. According to this plan Esro was to have contributed $1 million a year towards the cost of running the laboratory while the Italian government would have contributed $1.7 million. It became apparent two weeks ago at a previous Esro council meeting that this plan would have a rough passage when two member countries—Germany and the Netherlands—expressed concern over the $2.0 million a year that Esrin is currently costing Esro—this being a different objection to that first voiced against the continued support of Esrin, namely that the research carried out at the laboratory is not compatible with the future aims of Esro.

Esro still plans to use the buildings at Frascati and it was announced last week that the Esro technology dissemination service is to be transferred from Paris to Frascati in late 1972 or early 1973. Such a move is not likely to placate the Italians as their aim is to keep a viable Esro scientific effort within Italy.

As well as stopping support for Esrin the Esro council agreed that as from next July the organization's sounding rocket launching range at Kiruna in Sweden would be transferred to the Swedish authorities. These decisions will lead to employment problems for Esro and, although most of the employees at Kiruna will become employees of the Swedish government, it is far from clear what will become of the employees at Esrin—75 of whom are scientists. Esro currently employs 1,300 people—120 of whom are graduate scientists, 365 graduate engineers, 475 technicians and 340 administrative and other personnel. It is not known at present how the decisions will affect the number of employees although an Esro spokesman said last week "there is certainly no mass redundancy of any kind being planned".

The Esro council also agreed at last week's meeting on an overall plan for the organization until 1980. There will be an intensification of the applications satellite programme that will receive $70 million a year during 1974–80. Activities during the next few years will be concentrated on prototype development of aeronautical, navigation, meteorological and technological satellites and the budget during 1972–74 will be maintained at $283.6 million which will increase to $330 million during 1975–77.

MARS

No Cause for Concern

from our Soviet Correspondent

THE successful soft-landing on Mars, at a point approximately 45° S, 158° W—between the Electris and Phaethontis regions—of the instrument capsule from the Mars-3 probe has led to concern among some western observers about the possibility of biological contamination of the planet. The veil of secrecy surrounding the Soviet space programme has not helped to allay this disquiet, nor has the absence of any mention of biological experiments aboard the current probes in the preliminary press reports.

Writing in *Pravda* on December 6 (after the first batch of data and the short-lived video signals from the Martian surface had been received by orbital relay), Dr L. Mukhtin, Head of the Departmental Laboratory of Exobiology of the Institute of Space Research of the Soviet Academy of Sciences, stressed that exobiology is still part of the Soviet Mars programme. The search for life and for organic compounds, whether of biological origin or produced by ultraviolet radiation, will be carried out by future probes using "specially developed automata". The current probes, he says, are only "preparing the ground" for this important survey. If the results are negative, and "a strict proof of the absence of life on Mars" is obtained, this will be of equal scientific importance, "giving the possibility in the future of carrying out biological experiments in the conditions of a completely sterile planet".

It seems clear, therefore, that the Soviet Laboratory of Exobiology considers the Mars-3 descent capsule not to be a biological hazard to the planet.

CHEMICAL INDUSTRY

Dow Europe Healthy

DOW EUROPE, a subsidiary of the Dow Chemical Company, is now one of the most profitable members of the Dow group. Since its creation in the early 1950s to provide the European and African markets with specialist products (agricultural chemicals, for example) it has evolved in such a way that it now accounts for 26 per cent of Dow's world sales (which are at present running at $2,050 million a year) and about 30 per cent of the company's profits.

The president of Dow Europe, Mr Z. Merszei, claims that the goal set in 1963 of a 10 per cent increase in earnings each year has only been missed once—in 1970. And he says that the financial results for 1971 will show that the rate of growth of profits has clearly recovered to its pre-1970 level. The financial director, Mr P. Stroebel, says that the increasing growth of the company at a time when others are tightening their belts is a consequence of fundamentally different attitudes within the Dow corporation. Although many companies direct their investment to increasing their share of well tried markets, he said, Dow was always trying to tap new ones. Dow's European showpiece, its plant at Stade, West Germany, will soon be the company's largest chemical complex in Europe, producing many of its basic chemical requirements such as chlorine and sodium hydroxide.

Over the years Dow has channelled about 6 per cent of its European investment into Britain where there are now two manufacturing plants, at Barry and King's Lynn. The company also recently announced the establishment at King's Lynn of an agricultural research centre at which thirty professional scientists will eventually work; its budget is expected to be about $1 million a year. Dow already has what are described as technical service laboratories at Horgen, Switzerland, but the King's Lynn centre will be the company's first fully fledged research laboratory in Europe.

INDUSTRIAL RELATIONS

Same Game, New Rules

C. A. PARSONS, the Newcastle engineering company, has once again issued dismissal notices to 33 employees who are members of the United Kingdom Association of Professional Engineers. The company originally dismissed the engineers last July when they refused to join the Draughtsmen's and Allied Technicians' Association which, by working to rule twice and striking once, won a closed shop agreement from Parsons in May 1970.

Mr Jack Hill, the most senior of the 38 engineers then involved, sued Parsons for wrongful dismissal and last month the Appeal Court declared in his favour. Mr Hill and UKAPE regarded it as a test case, but last week Parsons issued the new dismissal notices to the remaining engineers with periods of notice ranging from three to six months according to length of service. At the same time, new contracts were offered which include the taking up of membership of the AUEW—with which DATA has now merged—as a condition of employment.

UKAPE's reaction has been to apply to the newly established Industrial Relations Court for a sole bargaining agency on behalf of the engineers at Parsons. This means that the resolution of the dispute awaits the decision of the court some time next year. UKAPE is the first union to apply to the Industrial Relations Court, and the decision will be one of the first under the new law. The fact that UKAPE is a registered trade union under the Industrial Relations Act, while AUEW has deregistered, only complicates the issue.

The only comment that DATA and Parsons were prepared to make this week on the new dismissal notices is that they are honouring the closed shop that they both agreed to last year.

METEOROLOGY

Typhoon Troubles

from a Correspondent

ONE of the most absorbing lectures delivered at the Unesco seminar on the effect of wind on building and structure, held on November 22–26 at Manila, Philippines, was by Professor Sean Mackey, University of Hong Kong. He discussed work on a ten storey building on Hong Kong island that has recently been built specially to study the effects of strong winds—in particular typhoons—on tall structures. The building, at Cape D'Aguilar, faces the sea and is particularly open towards the north-east from where the strongest winds blow when typhoons approach Hong Kong. So far only one such storm has occurred since the trials commenced and although this particular typhoon did not produce wind speeds of more than 100 mph other storms in Hong Kong have given gusts up to nearly 150 mph.

The building, as shown in Fig. 1, is 100 foot tall and of exposed structural steel construction. The floors are made partly of reinforced concrete solid-slab construction and partly of composite construction with a solid-reinforced concrete slab roof. The building can be divided into four sections, each coupled together at every floor level so that in strong winds the whole building acts as one unit.

On the right of Fig. 1 can be seen the four 175 foot high towers upon which a total of 44 anemometers have been fixed—one at each of eleven different levels on each tower, which are situated about 200 foot to the north-east of the building. To the left of the four main towers can be seen two additional masts, forty foot high, upon which are installed a further six anemometers to measure turbulence decay between the main recording point and the nearest building face. The white spots on the building face shown in Fig. 1 are several of a total of 102 pressure cells mounted in the glass wall panels. Special electro optical tracking instruments together with seismometers are also used to record sway and vibration characteristics of the building.

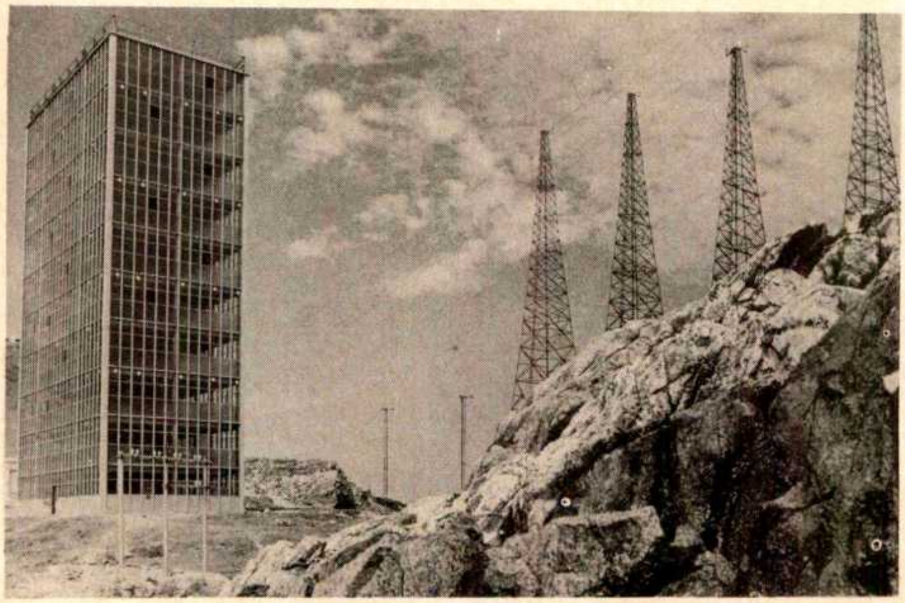

Fig. 1 General view of the testing site from the south-east

Although it is too early yet to assess results of actual typhoon winds the experiment and the Unesco seminar have drawn together meteorologists, architects, engineers and the building industry in an effort to draw attention to the urgent need to construct safe buildings which will stand up to the devastating effects of storm winds in typhoon prone areas.

EUROPEAN UNIVERSITIES

Common Problems

TEACHING ability should be taken into account when academics are considered for promotion, and inducements should be offered to them to ensure that they teach well. This was one of the themes that emerged from the Conference of European Rectors in Copenhagen last month, when representatives from the universities of twenty-five countries met to discuss the teaching role of the university.

Dr Albert Sloman, Vice-Chancellor of Essex University and president of the conference, said last week that he felt that all European universities are facing basically the same problems, but that they have reached them by different routes and therefore they might have to produce different solutions. For example, the call from university appointments officers and employers in Britain for more relevant courses is even louder in France where open access to university—as opposed to the selective access in Britain's universities—means that vast numbers of students are obtaining qualifications, particularly in the humanities and the social sciences, which are comparatively worthless as the staff–student relationship is too great for them to be well taught and the courses themselves are no real qualification for a job.

The conference, which has been meeting at six monthly intervals since Dr Sloman became president in 1969, is not an executive body, but simply meets for the rectors to exchange views; opinions differed most over the future role of universities. In his concluding remarks Dr Sloman suggested that it is very doubtful if society, with the cost of higher education rising, will allow every teacher the opportunity for substantial research. This could produce two types of institution—one heavily inclined to research and the other to teaching—as in Britain where both universities and colleges of technology and education exist. Alternatively there might be a single institution with people specializing in either teaching or research. Whichever is adopted Dr Sloman for one feels that there must be greater mobility of staff between research and teaching, as research should enrich teaching and teaching should enrich research.

NEW WORLD

Rogers Campaign Conquers Congress

by our Washington Correspondent

AFTER nearly a year of debate, with some of the most intensive lobbying ever devoted to scientific research, Congress has finally decided on a plan for organizing cancer research in the United States. President Nixon is said to be happy with the legislation and ready to sign it into law, thereby putting an end to a remarkable series of policy reversals by the Administration and making available $1,600 million for cancer research in the next three years.

One of the most remarkable aspects of the affair is that the debate has been almost exclusively concerned with the organization of cancer research. Throughout the long debate, it has been tacitly assumed that any amount of money can be spent wisely, and that there are many good ideas crying out for money to be put into effect.

The legislation now passed is substantially the same as the bill introduced into the House of Representatives by Congressman Paul G. Rogers in September, for whom the outcome of the debate is a great personal victory. As recently as July, it seemed that the support of Senator Edward M. Kennedy and President Nixon for a bill designed to make cancer research virtually independent of the National Institutes of Health would be strong enough to carry the bill through the House of Representatives. Only during the hearings held by Rogers's subcommittee was the biomedical community able to voice its fears about the dangers of such a measure.

Rogers's bill gained considerable congressional support in spite of powerful lobbying for the Senate bill by the American Cancer Society and by lobbyists connected with Mrs Mary Lasker, a New York millionairess and philanthropist who has in the past been instrumental in persuading Congress to increase appropriations for health research. The bill has survived his committee and the House of Representatives with only a few minor changes. More important, Mr Rogers has managed to keep nearly all his proposals in a conference committee set to iron out the differences in House and Senate passed bills.

As reported out of the conference committee and passed by Congress last week, the chief elements of the legislation are as follows.

The National Cancer Institute will coordinate all of the activities of NIH related to cancer, and it will remain functionally a part of the NIH. The Senate bill would have established a Conquest of Cancer Agency virtually independent of NIH.

The National Cancer Institute's budget will each year be submitted directly to the President, with opportunity for comment by the chairman of the National Cancer Advisory Board and by the Director of the National Institutes of Health. This measure, which is the same as that contained in the House bill, will give the National Cancer Institute some autonomy, and should ensure that its budget is kept at a high level.

A three man board will be set up to monitor the progress of cancer research, and to keep the President informed of any delays or blockages in funding or other bureaucratic difficulties that hold up research. The panel will be composed of three people who "by virtue of their training, experience and background are exceptionally qualified to appraise the National Cancer Program". Rogers managed to resist efforts in the conference committee to restrict the membership of the panel to the Director of NIH, the chairman of the National Cancer Board and the Director of the National Cancer Institute, although there seems to be some disagreement about whether those individuals would still be eligible to be members of the panel. If so, that would put them in the peculiar position of monitoring a programme for which they are responsible.

The legislation sets up fifteen new cancer research centres funded by block grants from the National Cancer Institute. Existing centres would also be able to receive block grants for research, and individual grants of less than $35,000 could be awarded by the Director of the National Cancer Institute on the basis of peer review, without first seeking the approval of the National Cancer Advisory Board.

A national Cancer Advisory Board will replace the present National Cancer Advisory Council. This is the only major provision contained in the Senate bill that survived the conference committee, and its effect will be to make the advisory body slightly more political. As at present constituted, the National Cancer Advisory Council consists chiefly of scientists and physicians appointed by the Secretary of Health, Education and Welfare, but the new legislation sets up a board consisting of twenty-three members appointed by the President. *Ex-officio* members would be the Secretary of Health, Education and Welfare, the Director of the Office of Science and Technology, the Director of NIH, the chief medical officer of the Veterans Administration and a medical officer designated by the Secretary of Defense, and the remainder of the places would be divided among scientists and laymen in the ratio of two to one. Apart from advising on overall policy for the National Cancer Program, the board will provide a report for the President and Congress each year on the progress of the programme.

One interesting aspect of the workings of the new bill will be the interplay between the National Cancer Advisory Board and the President's Cancer Panel, both of which are charged with the task of overseeing the cancer programme and both of which are essentially political bodies. Their relationship to each other is at present unclear, but there is bound to be some overlap.

SICKLE CELL ANAEMIA

Senate Prescription

by our Washington Correspondent

HAVING decided how to organize cancer research, Congress is now turning its attention to sickle cell anaemia—another disease ripe for an injection of Federal funds. Last week, the Senate decided to give $142 million over the next three years to programmes designed to combat the debilitating effects of the disease through research, and treatment, and to genetic screening and counselling aimed at cutting down the frequency with which it occurs. The Senate's deliberations on the legislation were marked by uncharacteristic alacrity, for the bill was passed only two months after it was first introduced by Senator John V. Tunney of California (see *Nature*, **233**, 517; 1971).

The disease is believed to afflict some 50,000 Americans, almost all of them black. Sickle-cell anaemia is the product of a recessive gene, which means that only homozygotes are frankly affected. Carriers of the sickle-cell trait, heterozygotes, are, however, partly protected against malaria, which explains the frequency of the gene among the descendants of the West African negroes in the United States. Some 2.5 million people carry the recessive sickle cell gene. The Senate's programme is therefore directed principally towards setting up genetic screening and counselling centres to identify couples whose children may be at risk, and another important part of the legislation is the provision of $42 million over the next three years to support research into the diagnosis, treatment and control of the disease.

Senator Edward M. Kennedy's public health subcommittee, which handled the legislation, was evidently impressed by witnesses who described the results of treating sufferers of sickle cell anaemia with urea or cyanate compounds. Such treatment is essentially aimed at overcoming the so-called sickle cell crisis—the painful and debilitating symptom of the disease caused when the red blood cells lack oxygen and form themselves into the sickle shape, severely restricting the flow of blood to tissues—but it is the subject of heated debate among many physicians. The committee report talks of a possible breakthrough in this area, and the bill authorizes the Department of Health, Education and Welfare to spend $5 million on research in 1973, $10 million in 1974 and $15 million in 1975.

Since the cause of the disease is genetic, it is incurable (in spite of a curious phrase which crept into the committee report to the effect that "further work in the field of genetic engineering also offers scope in the struggle to conquer this crippling malady"), and the Senate's bill therefore lays considerable emphasis on the provision of screening and genetic counselling centres to pinpoint carriers of the sickle cell trait and to advise couples who both carry the trait of the risks of bearing children who have the disease. Kennedy's subcommittee in fact increased the provision for setting up such clinics by the Department of Health, Education and Welfare by bumping up the funding to $25 million in 1973, $30 million and $40 million in 1975, chiefly on the basis that it would cost about $60 million to establish only ten such centres.

The bill also sees a role for the Department of Defense and the Veterans Administration in the fight against sickle cell anaemia, authorizing the defence department to conduct a screening programme, and giving the Veterans Administration a total of $12 million over the next three years for research.

If a similar bill is passed by the House — companion legislation was introduced by the District of Columbia delegate Walter Faunteroy and Mr Paul G. Rogers's health subcommittee has already conducted hearings on the bill —the Administration could be put in something of an embarrassing position. It was President Nixon who set the ball rolling in his health message to Congress last February, when he referred to the "shameful fact that the causes of this disease have been largely neglected throughout our history", but the bill that he is now likely to get back from Congress will contain expenditures many times greater than the present $6 million a year that is devoted to research, treatment, screening and counselling. Since there have already been many charges that the disease has been neglected because it is confined chiefly to blacks, the Administration would find it very difficult to oppose the legislation, even though Nixon now seems to enjoy testing his muscle with Congress over all sorts of legislation.

Short Notes

Ocean Dumping

The Senate agreed recently, by a vote of 73 to 0, to a bill designed to prohibit unregulated dumping of wastes into the oceans around the United States. The bill is in most respects the same as that passed in September by the House of Representatives, except that a provision designed to set up marine sanctuaries in some ocean areas has been removed. The designation of marine sanctuaries was intended by the House of Representatives to preserve intact areas of ocean for ecological, recreational or aesthetic reasons, and it would have led to the control of activities such as oil drilling in the designated regions. The provision was opposed in the Senate because the sanctuaries would have been set up in international waters—a suggestion to which senators objected because it may violate international law and also it may be viewed by other countries as "creeping jurisdiction" over areas of the high seas. The Administration also opposed that part of the House bill because it would have cost about $10 million to institute.

Nutrition

When Dr Robert B. Choate, a nutrition consultant, told a Senate Committee last year that many leading brands of breakfast cereal are over-advertised and under-nutritious, his revelations were greeted with scorn from the multi-million dollar industry (see *Nature*, **227**, 548; 1970). Nevertheless, while trying to belittle Mr Choate's analyses, the industry has been busy reformulating its products, and Mr Choate recently published a revised chart showing that twenty-six of the previously non-nutritious products have been considerably fortified with nutrients. Two of the most heavily advertised brands—Kellogg's Corn Flakes and Kellogg's Rice Krispies—are, however, among the bottom 10 per cent of all breakfast products in nutrient value, and on Mr Choate's analysis, can still be considered as "empty calories". The Food and Drug Administration has been developing nutrient guidelines for cereals for the past eighteen months, but "industry pressure and the lassitude of academia make us wonder whether the Food and Drug Administration will ever establish nutrition guidelines which can serve as a basis for ethical advertising slogans", Mr Choate tartly remarked.

Shuttle

A series of meetings was held recently between officials of NASA and the European Space Conference to discuss possible areas for cooperation on the post-Apollo space programme. The meeting is said to have produced a list of projects on which Europe and the United States may be able to cooperate. They include major responsibility for development of the space tug, sub-systems of the shuttle and supporting studies in related technology areas. It is now up to members of the European Space Conference to select specific projects on which to cooperate, and another meeting has been fixed for February for further discussions.

AEC and the Environment

Proposed amendments to the Atomic Energy Commission's regulatory procedure, published in the Federal Register recently, further extend the agency's control over the environmental consequences of building nuclear power plants. The AEC is intending to prohibit the clearing of land and other site preparations, such as construction of non-nuclear facilities such as turbine buildings, until a construction permit has been issued. The chief effect of the new regulations, which are at present open to public comment, would be to make such activities a part of the review of the environmental impact of a proposed plant.

Arms Race

The Federation of American Scientists, a consistent and vocal critic of the arms race, last week proposed that the President of the United States must have the approval of Congress before unleashing nuclear weapons in a first strike situation. The federation, which has always been opposed to the first use of nuclear weapons, has proposed this policy in conjunction with the War Powers Act introduced into Congress recently by Senators Javits, Stennis and Eagleton. The federation believes that such an arrangement would have the advantage of building into the nuclear arsenal an extra safeguard, and it would also have the added advantage of reducing international tensions during crises such as the Cuban missile crisis, since the first use of nuclear weapons by the United States would be ruled out unless Congress had given its express approval.

Preparation for a Rumpus

In the next few weeks *Nature* will publish a series of comments on the Dainton and Rothschild reports recently published in *A Framework for Government Research and Development*. The first is by Professor M. Swann, Principal and Vice-Chancellor of the University of Edinburgh.

THESE two reports make a fascinating contrast: Rothschild, on the one hand, wearing a loud check, thumps everybody and everything in sight and hurls around vulgar, academically disagreeable phrases like the "customer/contractor principle", in staccato fire. Dainton, on the other hand, in a well-cut, dark suit, analyses soberly and reasonably the troubles of a piece of the scientific establishment, in tones reminiscent of a professional man to his well-to-do client. No wonder there is going to be a rumpus.

In the light of the extensive leakages that have been seeping round the scientific world in recent months, I was certain that I was going to be a staunch Daintonite. Now that I have read the reports, and thought about them, albeit for not as long as I would like, I confess to thinking that the path of true wisdom for the well-being of science and society in Britain, lies somewhere midway between the two—perhaps even a little nearer Rothschild than Dainton. I don't expect this to be a popular point of view in academic circles.

One should not, of course, speak of the research councils in the plural. They vary enormously. NERC has been going for so short a time that one can only say it has made a good start with a difficult and diverse team. The ARC on the other hand, while it has indeed paid for itself many times over with Proctor Barley and other things, has been inviting trouble by failing in large measure to help and encourage agricultural and veterinary research in universities, and preferring to set up large specialist institutes which simply ask to be taken over by ministries. Ironically, Rothschild himself was once chairman of the ARC.

The real reputation of research councils rests on the achievements of the MRC and more recently the SRC. These are deeply impressive, and are envied and imitated the world over. These structures must not be dismantled. But (and having served on both councils, I know) their policies, by the very nature of their structure, are determined far more by the interests and demands of academic research workers than by the needs of society. There is no harm and on the contrary much good in this. Scientists know where science is going, in a way that ministries and society do not. Research councils can, and do, present society with benefits that no customer would ever have thought to ask for from his contractor.

It does mean, however, that research councils, concerned, as laid down in their charters and as their structures ensure, to support research of timeliness and promise, find great difficulty in stimulating work that meets some immediate social need but fails to attract good research workers. As an example, years ago, when I was on the MRC, some of us were concerned to stimulate more dental research (then, as now, slender), on the grounds that dental treatment cost the nation some hundreds of millions of pounds. We failed, I fear, to make any impact on the problem, and I am not aware that our successors have been markedly more successful. Given the research council structure, these are intractable problems not to be solved simply by the optimistic policy-making of a restructured Council for Scientific Policy.

Turning to Rothschild, I think it is unfortunate that he has put forward his proposals at a time of financial stringency and that he has put all his emphasis on the customer/contractor relationship, which I believe to be, in reality, the secondary consequence of a much more fundamental and acceptable reform that he proposes.

Had times been less hard, so that he could have left the research council budgets intact, I doubt if the academic/research council world would have objected to what he proposes. On the grounds that it would have meant more science, and more power for scientists, they would probably have welcomed it. It is not his fault that things have turned out otherwise. We have to accept at this moment a total science budget that is all but static.

My second criticism, however, is Rothschild's fault—in his presentation. I believe that his real contribution is to propose a structure, spreading through most if not all the departments of government, that builds in scientists, not in some pallid backroom advisory capacity, but in positions of influence.

This cannot be achieved, however, unless the departmental scientists can themselves call for research that will solve the departmental problems. And this in turn implies something like the customer/contractor relationship.

In another way, if we adhere too closely and universally to a research council structure that was expressly (and for good reason) designed to keep science and the scientists detached from the governmental structure, we can hardly be surprised that the governmental structure remains detached from the scientists. Rothschild wants to alter this, and he is right. But we must see that the civil servants do not, wittingly or unwittingly, torpedo his good intentions. Then we should have the worst of every world.

While I accept that some transference of research council budgets to ministries is essential, in a time of financial stringency I am concerned that the transfers should not be such as to shatter the research council structure, which undoubtedly, is far too valuable to lose. Moreover, if it is right that there be a 10 per cent surcharge on contracts for basic work, as I am sure it is, then it is surely also right that research councils be encouraged and allowed to do applied work on their own initiative. They may, after all, see the problems more clearly, and commission the work more skilfully themselves. I suggest, therefore, that the transition be decidedly more cautious, and initially smaller than Rothschild allows.

To sum up, I can do no better than say that the Green Paper recalls vividly the days when I and others, before our paths diverged, used to collaborate in research with Rothschild, on the mechanisms of fertilization in the sea-urchin egg. This was a hilarious business, conducted in marine biological stations around the world, and involving much noisy argument. It resulted in quite a lot of joint scientific papers. Sometimes one of us wrote the first draft and sometimes Rothschild did, in a style indistinguishable from his current report (doubters may care to look at his book on fertilization). In the latter event, even more noisy argument was needed to convert his first draft into a smooth acceptable manuscript. But we liked to think that the end results were good. And so perhaps they could be on this occasion.

NEWS AND VIEWS

Networks in Nature

THE use of analogy has for so long been part of the fabric of scientific method that the degree to which the very language of natural law is imbued with half-assimilated references of a historic or picturesque nature is apt to be forgotten. Sometimes the allusion is hardly more than metaphorical, sometimes it is completely misconceived; occasionally it embodies logical interrelationships of an extremely penetrating kind. In theoretical physics, where perhaps formal analogies stand out more clearly than elsewhere, their exploitation can be a matter of considerable subtlety, for a similarity between the equations governing experimentally separate phenomena can sometimes extend deeply into the more yielding sub-structure of hypothesis and thought experiment which lies beneath them. A careful study of this kind of interrelationship may then lead to insights into both fields which would hardly have been possible were they to be treated in isolation.

One of the most striking and fruitful of all interdisciplinary analogies—that between electrical networks and thermodynamic systems—has been the subject of increasing activity in recent years and is treated in an extensive article by Oster, Perelson and Katchalsky in this issue of *Nature* (page 393). Although "equivalent circuit" representations of macroscopic mechanical and microscopic accoustic and rheological systems have been utilized for many years—not least in the analogue computer—this aspect, though of practical importance, touches only superficially the heart of the matter. The deeper level, at which one considers the nature of the dissipative process in circuit elements, the interplay between reversible (reactive) and irreversible (resistive) energy flows, the symmetry of input and output and so on, has only been examined in comparatively recent times and this largely due to the work of a single man, Josef Meixner in Aachen.

When Meixner, some ten years ago, began his reappraisal of the connexion between thermodynamics and network theory (*J. Math. Phys.*, **4**, 154; 1963), little was appreciated—beyond certain themes which could be traced back to Maxwell, Kelvin and Heaviside—of the precise way in which each of these considerable bodies of knowledge held implications for the other. Even now it is necessary to caution the reader conditioned by classical heat theory that an electrical network exchanging energy with its surroundings is a thermodynamic system in its own right, so that its treatment is more by extension of than analogy with conventional results. Meixner's findings, which were also relevant to distributed parameter systems and electric fields (*Acta Physica Polonica*, **28**, 113; 1965), proved to be far more than textbook curiosities, for, in addition to providing particularly transparent examples of the essential identity of the Onsager-Casimir reciprocal relations of classical non-equilibrium thermodynamics and the reciprocity of the admittance matrix for networks, they led eventually to a fundamental reconsideration of the usefulness of the concept of entropy in non-equilibrium physics.

The central feature of Meixner's approach is the concept of "passivity" in a system and the importance of this is reasserted by Oster, Perelson and Katchalsky in the related language of Tellegen's theorem for networks. Though at first sight the passivity property seems to be simply an expression of energy conservation in a system without sources, it can be shown to imply deeper stability conditions and thus connect with the second as well as the first law of thermodynamics. By bringing to bear the now well-developed apparatus of generalized network theory, Katchalsky and his colleagues have been able to point the way to a number of extensions of the Aachen formulation which promise considerable advances in both practical and theoretical terms.

First, Katchalsky and his colleagues show, with examples from membrane systems, how the techniques developed in engineering systems theory might be applied to the extremely highly connected and inhomogeneous patterns of forces and fluxes which are characteristic of cell biology. For this they introduce an element unfamiliar in physico-chemical thermodynamics—the idealized "transducer", a transformer-like unit with possibly non-linear response. They also explain how some of the graphical techniques developed by engineers can enormously simplify the writing of network equations, emphasizing, however, that a good diagrammatic notation can be far more than a book-keeping scheme or an algorithm for recovering these. As in other branches of physics, diagrams may here provide a calligraphy, so to speak, for the topological relations embodied in the connectedness of the system, properties which may be obscured in the bare equations themselves.

The results of Oster, Perelson and Katchalsky are by no means limited to prescriptions for codifying network structure in physico-chemical systems; in fact they emphasize two further aspects which seem to go significantly beyond the established concepts of non-equilibrium thermodynamics. They accept the inevitability of non-linear constitutive relations, which have always been shunned by physicists, showing how these can be accommodated, at least formally, in a Hamiltonian-like system related to the so-called Brayton-Moser equations for networks, and, in what seems to be a major step, explain how the reciprocity properties of networks—which in electrical terms refer literally to interchange of input and output—can be taken over into thermodynamics to give a non-linear generalization of the Onsager-Casimir reciprocal relations. For non-linear passive systems the key quantity in this turns out to be the Jacobian of the force-flux transformation, which in turn implies an integrability condition and the existence of state functions such as internal energy.

As the authors are at pains to point out, even such sophisticated treatments remain phenomenological in character, in network theory just as in conventional thermodynamics. One must still put in not only the parameters of the system and the forms of the constitutive relations governing the junctions, but, in practice, also make implied postulates about the level at which system elements are known in structural detail and below which they appear simply as "black boxes".

It is in this aspect that the doubts raised by Meixner about the usefulness of "entropy" as a function to characterize macroscopic non-equilibrium systems arise. His conclusion is quite unequivocal: "Unsere Behauptung ist nun, dass die Definition einer eindeutigen Entropie für Vorgänge nicht nur bisher nicht geschehen sondern sogar unmöglich ist, falls man nur makrophysikalische Überlegungen zulässt, d.h. die Existenz der atomistischen Struktur der Materie ignoriert." ("Our assertion is thus, that the definition of an unambiguous entropy for (non-equilibrium) processes not only has not so far been achieved but is actually impossible, so long as only macroscopic considerations are admitted, i.e. the existence of an atomic structure of matter is ignored.") (*Rheologica Acta*, **7**, 8; 1968.)

Although such a conclusion is strongly suggested by statistical mechanics Meixner's conviction is based on the disarmingly simple observation that a two-terminal resistive network can be reproduced—so far as its input-output characteristics are concerned—by an infinite variety of equivalent "black boxes" containing inductances and capacities. Because these can never be distinguished without some process of opening the boxes and examining their internal structure, neither can the irreversible (resistive) dissipitation of energy be properly separated from the reversible (reactive) energy flow. By the same token the dissipative processes in thermodynamics cannot be unequivocally characterized, except at a sub-microscopic level, in fact only at the point where the continuum approach must give way to an atomistic statistical mechanics.

Thus macroscopic thermodynamics comes up against something like the information-theoretic barriers which are accepted, in somewhat better grace, by the users of black-box formulations in behavioural psychology and automata theory. Meixner has shown that the consequences of this are not irreparable and that an entropy-free thermodynamics may be constructed, at least for linear systems, using the passivity principle. It new seems reasonable to hope that the advances described by Katchalsky, Oster and Perelson may point the way to a similar development for non-linear thermodynamics before long.

Muscling In

MOTILITY, the ability to move, is one of that list of characteristics of living organisms which every schoolboy learns, or used to have to learn, by rote in his first biology lesson. Cells and other organisms exhibit movement at some stage or in some part during their life history and, perhaps not surprisingly, evidence is steadily accumulating which suggests that motility and contraction in many, indeed perhaps even in all biological systems, has a common molecular basis.

Striated skeletal muscle of animals is, of course, the classic, most accessible and most thoroughly analysed contractile apparatus of organisms. It now seems beyond dispute that muscular contraction depends on the interaction of polymers of two contractile proteins, actin and myosin, which are arranged in interdigitating arrays of filaments. At least, when a striated muscle contracts projections from the myosin filaments cyclically attach to, and detach from, adjacent actin filaments in such a way that transient actomyosin bridges pull the actin filaments into the myosin filaments with the net result that the muscle shortens.

Armed with the knowledge that actin and myosin comprise the basic contractile machinery of muscles, biologists have, naturally enough, repeatedly searched for either or both of these proteins in other tissues, cells and organelles which move. And as the techniques for extracting and characterizing proteins have improved actin-like and myosin-like proteins have, sure enough, been identified with increasing frequency and certainty in all sorts of situations.

A few weeks ago, for example, Fine and Bray reported in *Nature New Biology* (**234**, 115; 1971) that as much as about 20 per cent of the total protein in chick neurones is an actin-like protein, which may very well be identical to skeletal muscle actin. They also find actin or actin-like proteins in chick embryonic lens, lung, skin, heart, pancreas, kidney and brain tissue. And in this issue of *Nature* (see page 410) Gawadi reports the location of actin which has been observed in the mitotic spindle apparatus; he believes it occurs in filaments running parallel to the long axis of the spindle but not closely associated with the spindle microtubules. Behnke, Forer and Emmersen (see page 408) reach much the same conclusion about the distribution of actin or actin-like protein in the meiotic spindle of crane fly spermatids and they also report the presence of this muscle protein in crane fly sperm tails. Other workers have claimed to detect actin or myosin-like proteins in mitochondria, chloroplasts and cilia and, recently, Adelstein, Pollard and Kuehl (*Proc. US Nat. Acad. Sci.*, **68**, 2703; 1971) report isolating both actin and myosin-like proteins from thrombosthenin, the complex of contractile proteins in human blood platelets; these examples by no means exhaust the list.

It has to be admitted, of course, that more often than not the criteria for the identification of these two proteins in novel situations are not rigorous enough to satisfy completely the standards set by muscle biochemists. But where serious attempts have been made to compare skeletal muscle actin and actin-like proteins from other sources—the experiments of Fine and Bray are a case in point—few differences have been detected, although, as Fine and Bray themselves comment, nothing short of the total amino-acid sequences of actins from different sources can establish their complete identity or the extent of differences. That proviso notwithstanding, however, the sweeping generalization that actin and myosin-like proteins may universally provide the molecular basis of motility in biological systems becomes almost daily more attractive.

TAXONOMY

Postgraduate Course

FROM next October an MSc course in animal taxonomy will be organized by the Department of Zoology and Applied Taxonomy at Imperial College, London, in collaboration with its neighbour in South Kensington, the British Museum (Natural History). This will be the first postgraduate course devoted specifically to animal taxonomy; it will also be the first linkup between a British national museum and a university department to produce a postgraduate course in the biological sciences.

PRIMATE BEHAVIOUR

Focus on Function

from a Correspondent

USING a previously successful formula, the Primate Society of Great Britain and the Association for the Study of Animal Behaviour joined forces to hold a symposium on primate behaviour on November 25 and 26 at the Zoological Society of London. Three major research areas were covered: field studies of behaviour and ecology; laboratory manipulation of primate behaviour; and human ethology. In all of these areas, it is now clear that research workers have generally progressed beyond mere use of established terminology and the belief that such description constitutes scientific explanation. In most studies, functional relationships now form the focus of research.

Following the example of Dr John Crook (University of Bristol), many field workers are now concentrating on the relations between primate behaviour and the natural environment. This central interest was present in varying extents in contributions on the natural behaviour of the mouse lemur (Dr R. D. Martin, University College, London), the red colobus (Mr T. Clutton-Brock, University of Cambridge), the talapoin (Dr Annie Gautier, University of Rennes), and simian primates in Malayan forest (Dr D. J. Chivers, University of Cambridge). Recent studies demonstrate a clear correlation between general behaviour (particularly social structure) and environmental features such as food availability and food distribution. The precise techniques developed by Mr Clutton-Brock for investigating patterns of home ranges have destroyed the myth that forests are homogeneous areas of trees, and this kind of study will doubtless become increasingly important in the future. The data already available show that spatial and social systems of primates are adapted to key environmental factors in a highly sophisticated fashion. The study by Dr J. C. Rodman (Harvard University) of the orang-utan further brought out the point that many primate species exhibit local variations in social structure and home-range attachment. In Dr Rodman's study area, the orang-utans are sedentary, in contrast to those observed previously by John McKinnon in a different region.

The symposium also included two excellent studies on specific aspects of behaviour which have long required investigation: Dr J. Deag (University of Edinburgh) gave a graphic account of intergroup encounters in wild Barbary macaques, showing that these primates do (after all) exhibit a refined form of territoriality—so refined that a less careful observer might have overlooked it entirely. Dr M. J. A. Simpson (University of Cambridge), covering a different subject, provided an elegant analysis of male grooming relationships in a wild chimpanzee group. Male chimps spend more time grooming other males than females, and the high-ranking males groom most, although it is the subordinate chimp in any encounter which will groom longest.

The laboratory behaviour manipulators produced some extremely good contributions and there were distinct signs of greater appreciation of "natural behaviour" in these investigations. Dr R. P. Michael (Institute of Psychiatry, London) gave a lucid account of his team's research on hormonal control of sexual activity in female rhesus monkeys and neatly showed the potential calibre of long-term projects. His techniques permit quite detailed analysis of factors operating in mating activity, and one important observation is the occurrence of a point where the hormone-treated, castrated female is attractive to the male, but is not yet "interested" in him. This indirect demonstration of the action of female attractive scents ("pheromones") has been supported by precise studies of female vaginal secretions, including gas chromatographic analysis.

Providing a relief from many castration experiments, Professor D. Ploog (Max-Planck Institute for Psychiatry, Munich) gave an interesting review of communication in captive squirrel monkeys, bringing together various results from behavioural observation, recordings of vocalizations and experiments using cerebal radio-stimulation. The combination of techniques used in this ambitious study is now beginning to provide a detailed picture of the central nervous control of communication in this species. Professor R. A. Hinde (University of Cambridge) reported on his study of infant–mother) separation in rhesus monkeys, and showed that finely controlled intervention can yield precise data which may be swamped in more drastic experiments. It was surprising to learn that it is apparently less traumatic for the (6 month old) rhesus infant to be isolated from the cage group, including its mother, than for the infant to be left with the group after removal of the mother.

Dr J. P. Hess (University of Basle) described a detailed study of the sexual behaviour of the lowland gorilla in Basle Zoo. This study deserves a special note because of the virtual impossibility of observing such behaviour in the wild. Dr Hess backed up his data with a film which illustrated the striking invitation behaviour of captive gorilla females and demonstrated the finer points of mating behaviour.

The session on human ethology attracted particular interest and included an excellent lecture on human sexual dimorphism by Dr Corinne Hutt (University of Reading). After outlining some of the biochemical and physiological evidence for early sexual differentiation in human beings, Dr Hutt summarized her observations on early differences in behavioural development in human infants. The important question of cross-cultural comparison of human behaviour was broached by Dr N. Blurton Jones (University of London), who made a preliminary report on a combined study of Bushman and London children. Many qualitative similarities were seen in this study; but there were also many quantitative

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Black Holes against Neutron Stars

Is mass the single vital factor in determining whether a given star will evolve into a neutron star or a black hole? As stellar evolution theory has developed, the importance of the role taken by rotation has become increasingly clear, and it now looks as though this is particularly true at the end point of stellar evolution.

In next Monday's *Nature Physical Science* Sabatino Sofia presents calculations showing just how rotation affects these late stages of a star's life. If the rotational velocity of the star is high, then, as might be expected naively, a large amount of matter is shed during the evolution and the remaining core can settle down as a neutron star. But if the velocity is low, little mass can be lost and the core collapses.

The interesting question, of course, is just where the dividing line comes. According to Sofia, the condition for the formation of a neutron star turns out to be that the angular momentum of each element satisfies the inequality

$$L > \sqrt{10^6 \, GM_r}$$

where M_r is the mass interior to the element. But this is still only half of the required solution. Applications to real stars depend on knowing realistic mass and angular momentum distributions. By making the crude assumption that no angular momentum transfer occurs after a star leaves the main sequence, Sofia finds that for a 25 $M_\odot$ star an angular velocity of 4×10^{-6} cm s^{-1} is sufficient for stability, and that a 5 $M_\odot$ star is stable for angular velocities above 9.6×10^{-6} cm s^{-1}. These limits are unlikely to be more than two or three times smaller than realistic limits. Only very slowly rotating, massive stars can thus evolve into black holes.

differences. Mr P. K. Smith (University of Sheffield) complemented these studies with a demonstration of the use of penetrating statistical tests (principal component analysis followed by factor analysis), which provide a firm basis for analysing clusters of infant behaviour patterns. He confirmed Dr Hutt's observation that English children, at least, exhibit some highly significant sex differences. On a different tack, Dr A. Kendon (Bronx State Hospital, New York) gave a descriptive account of human greeting gestures, largely based on a film record of a party. This particular talk, however, illustrated the fact that human ethology is still hovering between the anecdotal and analytical levels. Systematic data analysis and presentation are necessary to convince sceptics that complex terminology reflects underlying behavioural mechanisms, rather than the verbal creativity of the observer.

MERCURY

In the Atmosphere

from our Geomagnetism Correspondent

THE recent public attention given to the levels of mercury in, for example, tuna fish and swordfish has led Weiss *et al.* (*Science*, **174**, 692 ; 1971) to investigate the complementary problem of whether or not the atmospheric content of mercury has increased in recent years and, if so, whether the increase may be attributed to man. On the face of it there is good reason for supposing that man's activities may have produced such an increase. The combustion of fossil fuels, the roasting of ores and the production of chemicals with mercury catalysts are all processes which could in theory lead to a significant rise in the mercury level, although there are also known natural processes which could contribute to such a rise. What Weiss and his colleagues have thus set out to do is to make quantitative estimates of what has been, and is, happening.

Their method has been to determine the mercury content of ice samples ranging in age from 800 BC to the summer of 1965. At the time of their formation ice samples record, and subsequently maintain in essentially unchanged condition, the composition of the atmosphere. Strictly speaking, the composition recorded is the composition of the materials which are washed out from the atmosphere by the relevant precipitation; but because rain effectively removes mercury from the atmosphere it may be confidently assumed that the mercury content of ice may be equated to the corresponding mercury content of the atmosphere. By analysing ancient ice samples and dating them using such methods as ^{210}Pb and fission product geochronology, oxygen isotope analysis or firn stratigraphy, it is thus possible to estimate the composition of the atmosphere as a function of time depending only on the availability of samples.

In this case the ice samples were taken from Greenland and Antarctica. The results indicate a significantly higher rate of deposition of mercury in recent years. Ice samples formed before 1952 had mercury contents ranging from 30 to 75 ng per kilogram with a mean value of 60 ± 17. By contrast, the mean value for the period 1952–1965 was 125 ± 52 ng per kilogram with a range of 87–230. The mercury content of the atmosphere has thus apparently increased by an average factor of two since early historic times.

To investigate the cause of this increase Weiss and his colleagues have attempted to calculate the relative contributions of mercury to the atmosphere from both natural and industrial processes. Clearly any such calculations must make many oversimplifying assumptions and the results can thus only be regarded as orders of magnitude; but in the sense that some of the computations may be made in different ways starting from different assumptions there are certain inbuilt checks on the validity of the results.

The flux of mercury from the continents to the atmosphere arising from natural processes is thus calculated by Weiss *et al.* to be in the range 2.5×10^{10} to 1.5×10^{11} per year. By contrast, the flux of mercury from the continents to the oceans by way of rivers is much less—a maximum of 3.8×10^{9} per year. Neither can industrial processes compete with the natural continent-atmosphere transfer, apparently. The mercury lost to the atmosphere in chlor-alkali production is estimated at 3×10^{9} g per year ; cement manufacture adds another 10^{8} g per year ; the roasting of sulphide ores could give another 2×10^{9} g per year ; and Bertine and Goldberg (*Science*, **173**, 233 ; 1971) recently showed that an upper limit of 1.6×10^{9} g of mercury per year can be released to the atmosphere through the burning of coal, oil and lignites.

Why, then, has the mercury content of the atmosphere recently increased by a factor or two? Weiss and his colleagues speculate that man is, in fact, responsible but not in the most obvious way. They attribute the natural transfer of mercury to the atmosphere to the degassing of the Earth's upper mantle and lower crust—a thesis supported by the fact that mercury is enriched in sedimentary compared with igneous rocks and the fact that atmospheric mercury concentration depends on barometric pressure.

INDUSTRIAL HEALTH

Exposure to Asbestos

from a Correspondent

ASBESTOS is an insidious pollutant. But because of its widespread industrial application as an insulator many workers are liable to be exposed to its effects. In a study of workers in a New England shipyard whose job was to cover pipes with an asbestos layer, signs

Role of Initiation Factor F3

IN *Nature New Biology* next week Ochoa and his colleagues, in two reports, describe their latest probings of the function of factor F3, one of the initiation factors responsible for catalysing the association between ribosomes, messenger RNA and the initiating species of aminoacyl-tRNA, fmet-tRNA$_f$, at the start of protein synthesis. Sabol and Ochoa show that factor F3 is not only required for the binding of messenger RNA to the small 30S ribosomal subunit at the beginning of translation but is also required for the dissociation of 70S ribosomes released from a messenger when they have completed a round of protein synthesis.

Sabol and Ochoa's experiments indicate that 70S ribosomes released from a messenger are dissociated when a molecule of F3 binds to the 30S subunit of the 70S ribosome. The released 30S subunit, with a molecule of F3 still attached, is then available to associate with another messenger molecule to form an initiation complex. Once this has happened the molecule of F3 is displaced as the 50S ribosomal subunit binds to the complex to form a 70S ribosome capable of completing the translation of the messenger. The liberated molecule of F3 meanwhile is free to dissociate another 70S ribosome running off the end of a messenger and so the cycle continues.

Factor F3 thus plays a crucial part in potentiating the 30S ribosome and Lee Huang and Ochoa report further evidence that different species of F3 factors exist in *Escherichia coli* which can discriminate between different species of messenger RNA and therefore regulate which are translated. They find that two F3 factors purified from *E. coli* infected with phage T4 and from uninfected cells differentially promote the translation of early and late T4 messengers and phage MS2 RNA. One factor promotes translation of MS2 and early T4 messenger RNAs and the other promotes translation of late T4 messengers.

of asbestosis were eleven per cent more common than in controls taken from other shipyard workers.

The disturbing feature of this report is that the pipe coverers were working in an environment where the exposure to asbestos dust was at about the recommended maximum level thought to be safe. This research is described in the *New England Journal of Medicine* by a group from the Harvard School of Public Health and the Boston medical school (**285**, 1271 ; 1971), and is an invaluable account of the condition of workers in an asbestos environment that is known from long term studies to have been more or less constant for twenty years.

There is no specific diagnostic test for asbestosis so that the diagnosis depends on the presence of symptoms such as shortness of breath on exercise, X-rays of the lungs, tests of respiratory function and clinical findings, particularly auscultation of the lungs for the character of the breath sounds and the occurrence of abnormal sounds. Other dust-induced lung diseases lead to similar signs and symptoms; the final diagnosis depends on a history of exposure to asbestos.

In the present investigation, the exposure to asbestos was not in doubt. What the investigators wished to discover was the extent to which the workers in an environment thought to be safe showed respiratory disorders attributable to asbestosis. To minimize the subjective elements the X-rays were examined independently by three radiologists, and criteria were established for the diagnosis of asbestosis based on the presence of a number of clinical abnormalities.

The control group was matched for age, duration of employment, height and weight, smoking habits, marital status, and location of residence. The pipe coverers had been employed in the shipyard for an average 17.4 years and the controls 17.1 years.

The striking result of the survey is that of 101 pipe coverers (compared with 94 controls), thirty-eight per cent of workers with twenty years of cumulative exposure had asbestosis.

Although slow in onset—asbestosis was never diagnosed in men with less than ten years' cumulative exposure —asbestosis progresses to a severely disabling and ultimately fatal disease impairing the function of the lung. Small fibres, when inhaled, can penetrate the tissue of the lungs causing reactions which lead to destruction of normal lung tissue. Apart from being itself a lethal disease, asbestosis lowers the resistance to pulmonary tuberculosis and increases the liability to cancer of the lung.

This painstaking survey of the shipyard will no doubt play an important part in the establishment of threshold limits for exposure to asbestos dust, and as the *New England Journal of Medicine* says in an editorial, the threshold limit value should be lowered far below some recent proposals.

DNA REPLICATION

RNA Primer

from our Cell Biology Correspondent

A LITTLE may be known about the biochemistry of the semi-conservative replication of DNA but, as a glance through the contents tables of the current batch of journals shows, that is not for want of trying. Brutlag, Schekman and Kornberg (senior), for example, report (*Proc. US Nat. Acad. Sci.*, **68**, 2826 ; 1971) an intriguing set of observations which they believe indicates that RNA polymerase is involved in the initiation of replication of single standard, circular M13 DNA; they suggest that the RNA polymerase may act by providing an RNA primer molecule onto the 3′ hydroxy group of which DNA polymerase initiates DNA synthesis.

Brutlag *et al.*'s observation is simply that the conversion of single stranded M13 DNA to a double stranded replicative form and the subsequent replication of the replicative form in *Escherichia coli* is blocked by rifampicin, a specific inhibitor of *E. coli* RNA polymerase. Furthermore, as expected from this observation, this block to replication of M13 DNA is not seen when *E. coli* cells, which have an RNA polymerase mutated to resistance to rifampicin, are infected in the presence of the drug.

Not so long ago the suggestion that an RNA chain might prime DNA polymerization would certainly have been viewed askance, but now that Baltimore's group (Verma *et al.*, *Nature New Biology*, **233**, 131; 1971) have shown that reverse transcriptase initiates DNA synthesis, directed by an RNA template, on an RNA primer such a suggestion is unlikely to cause any great stir. Indeed, Verma *et al.* themselves suggested that DNA polymerases like reverse transcriptase might initiate DNA synthesis with an RNA primer.

In the same issue of the *Proceedings* (*ibid.*, 2839) Inselburg and Fuke report that minicells produced by the mutant strain of *E. coli*, P678–54, which carries the colicin E1 genome, contain colicin E1 DNA but no cellular DNA. The circular colicin E1 genomes in these minicells seem to continue to replicate and various catenated and replicating E1 DNA molecules can be extracted. According to Inselburg and Fuke the behaviour of these colicin DNA molecules when sedimented in sucrose and caesium chloride-ethidium bromide density gradients indicates that both Cairns-type double forked circular molecules and Rolling circle-type circular molecules with linear tails are present.

Elsewhere, Strätling and Knippers (*J. Mol. Biol.*, **61**, 471; 1971) relate their latest observations of DNA synthesized by DNA-membrane complexes isolated from polA$^-$ mutant *E. coli* cells. These cells lack DNA polymerase I (Kornberg enzyme) activity but have at least one

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Location of Calcium Ions in Striated Muscle

STUDIES on the structure of muscle filaments have gradually made clear a general framework for hypotheses on the mechanism of muscle contraction. The basic force-developing step is still elusive, however, and there are also several features about the "switching on" process about which very little is certain. It is useful therefore to have any new information on these events, and a report by Yarom and Meiri of the Hebrew University, Jerusalem, in next Wednesday's *Nature New Biology* describes some experiments designed to fix the location of the chief storage site for calcium ions.

Potassium pyroantimonate has previously been shown to precipitate calcium in cardiac muscle, and Yarem and Meiri used this method to precipitate and thus locate the calcium ions in striated muscle. The muscle was treated with a solution of sucrose, potassium pyroantimonate and the fixative osmium tetroxide at *p*H 7.2. Electron micrographs of longitudinal sections of these muscles showed stain between the myofilaments and it concentrated in particular along a line in the I band known as the N_2 line. The two N lines are densely staining lines in the I band and the N_2 line differs from the N_1 in that the distance of the N_2 line from the Z lines increases with sarcomere length. The muscles were then tetanized electrically through the nerve and fixed during the tetanus plateau. Longitudinal sections from such muscles did not show predominantly stained N_2 lines, but the stain was dispersed along the myofilaments. Additional muscles were treated with EGTA, a strong calcium chelating agent, and were then treated with pyroantimonate and the osmium tetroxide fixative. No myofibrillar deposits were observed in longitudinal sections of these muscles.

Thus, Yarom and Meiri suggest, it is possible that the N_2 lines are sites for the storage of intracellular calcium.

other residual DNA polymerase activity, DNA polymerase II, which can be isolated free of membrane and template. The DNA-membrane complex obtained from these cells continues for short periods to synthesize DNA *in vitro* (whether this synthesis is brought about by DNA polymerase II is an open question). The DNA made *in vitro* sediments with the bulk template parental DNA until the protein component of the complex is removed. After the removal of the protein the DNA made *in vitro* sediments as fragments ranging in sedimentation coefficient from 10S to 25S. At least some of these fragments, the 10S fraction in particular, seem to contain molecules in which parental and DNA sequences made *in vitro* are covalently linked while the remainder of the fragments seem to comprise parental DNA hydrogen bonded to DNA made *in vitro*. Moreover, kinetic studies indicate that the covalent linkage of parental and *in vitro* DNA chains is transient.

Strätling and Knippers believe that these observations indicate that parental DNA is nicked by endonucleases to produce free 3′ hydroxy termini which not only allow free rotation of the DNA strand but also serve as a primer for DNA synthesis. They further suggest that the parental/progeny molecules so produced are cut by endonucleases to separate parental from newly made DNA and then the two sorts of DNA fragments must be relinked to form continuous parental and progeny strands.

Strätling and Knipper's data, as they comment, are consistent with Haskell and Davern's model which envisages that DNA replication involves the introduction of nicks ahead of the replication fork, with the nicked pieces serving as primers for DNA synthesis. The recent experiments of Werner (*Nature*, **230**, 570; 1971) also indicate that progeny and parental DNA chains are transiently linked by covalent bonds, although Werner interprets his findings differently. In short, it seems that during *E. coli* DNA synthesis parental and progeny sequences are linked but how and why remains to be unequivocally explained.

HAEMOGLOBIN

Models for All Tastes

from our Molecular Biology Correspondent

As to the choice of a kinetic scheme for haemoglobin oxygenation, most workers in the field will still prefer, like H. L. Mencken's politician, to sit on the fence while keeping both ears to the ground. Although the structural differences between the oxygenated and deoxygenated states have been defined in minute detail by Perutz, who was able to infer from them many features of the mechanism of oxygenation, this has been insufficient to quell the wrangle about which of the several feasible mechanistic models best fits the equilibrium and kinetic data.

MacQuarrie and Gibson (*J. Biol. Chem.*, **246**, 5832; 1971) have gathered some interesting evidence from a comparison of carbon monoxide binding rates and release of the cofactor, 2,3-diphosphoglycerate, which binds in a ratio of one molecule per haemoglobin tetramer to the deoxygenated form only. More exactly, they have used a fluorescent analogue of diphosphoglycerate, a hydroxypyrenetrisulphonate, which competes with the cofactor for the single site, and has a qualitatively identical effect on the oxygen uptake curve. The binding of this form is easily measured, for when it is bound its fluorescence is quenched by the haem groups.

When carbon monoxide is introduced into a solution of haemoglobin containing some of the cofactor, the kinetics of binding of ligand and release of cofactor can be simultaneously measured by fast spectroscopy. It is at once apparent that the two processes follow different rates. This leads immediately to the conclusion that intermediate oxygenation states occur in significant concentration. MacQuarrie and Gibson then go on to interpret their results in terms of alternative ligand binding mechanisms, assuming only that there are not more than two affinity states in respect of the cofactor. They fit the rate data first in terms of an Adair model, with four sequential binding reactions, in which the liganded conformational state reacts rapidly with carbon monoxide and does not bind the cofactor. The cofactor, in this scheme, is released after the attachment of the third haem ligand. A least-squares fit of both the carbon monoxide and cofactor binding curves shows that this formation is capable of satisfying the observations within the error of the experiment. If, on the contrary, one assumes that the cofactor is released after binding the second ligand, the fit is much worse (though one

The Lymphocyte Trap Sprung

The jargon of the cellular immunologist contains words such as population, microenvironment, migratory, which would be perfectly proper on the lips of an ecologist. This perhaps provides a clue to some of the present trends in cellular immunology because to an ever increasing extent lymphocytes are being studied in relation to their environment. It is quite feasible to think of lymphocytes as organisms of which the behavioural, morphological and functional characteristics can be arranged in relation to their environment in the intact vertebrate. Such a concept stresses that the lymphocyte in its most interesting form is abundantly alive. The old days of the strictly morphological approach based exclusively on the perusal of long dead slices of tissue are happily past.

In *Nature New Biology* next Wednesday (December 22), Zatz and Lance present a communication entitled "Lymphocyte Trapping in Tolerant Mice". This study, with its undertones of polecats and the frozen North, concerns the phenomenon of retention of migratory lymphocytes in lymphoid organs which are involved in responding to an antigenic stimulus. The method is simple. Lymphocytes are labelled with ^{51}Cr *in vitro* by incubation in an appropriate solution of "hot" sodium chromate. Subsequently, the labelled cells are injected intravenously into mice at various times after antigenic stimuli. It is a reasonable approximation to say that for a day or so the amount of radioactivity found in various lymphoid organs of the body will be an accurate indicator of the presence of the labelled cells. The lymphoid organs are always harvested 24 h after the injection of labelled cells.

Lance and his associates have previously demonstrated that in lymph nodes which drain the site of application of a foreign skin homograft more of the injected cells were found than in comparable nodes which drain the site of a skin autograft. The maximum differential between the two kinds of node was observed at about the tenth day after application of the skin homograft, before the graft itself is rejected. The functional significance of the phenomenon cannot at the moment be specified but in their most recent experiments Zatz and Lance find that in parental mice rendered tolerant by neonatal injection of F_1 spleen cells trapping does not operate in the lymph nodes draining the site of an applied (and tolerated) skin homograft.

In other studies it has been shown that some degree of engorgement of lymph nodes can follow the introduction into afferent lymphatics of some of the products of stimulated lymphocytes (Kelly, R. H., *Clin. Exp. Immunol.*, in the press, 1972). It is tempting to suppose that some such mechanism is operating (or failing) in the lymph nodes of the mice of Zatz and Lance. It will be interesting to learn when and with what intensity the trap operates in animals which have been injected with either immune or normal cells in order to break the tolerant state.

is throughout concerned only with deviations of up to a few per cent at worst, because three variables are available for fitting, and the calculation is insensitive to the last binding step).

For the all-or-none, allosteric, model of Monod, Wyman and Changeux, using for the three adjustable parameters the equilibrium constant relating the high and low affinity states of the protein, the ratio of their ligand affinities and one of the two rate constants demanded by the model, the fit is again poor. It may be noted that the release of diphosphoglycerate after oxygenation of the third haem was earlier deduced by Tyuma *et al.* (*Biochem. Biophys. Res. Commun.*, **43**, 423; 1971), simply from a comparison of the parameters defining the oxygen dissociation profiles in terms of the Adair equation, in the presence and absence of the cofactor. They were able to show moreover that the last oxygenation step could be quantitatively identified with the reaction of an isolated β-chain.

These results then are without doubt strong arguments in favour of one type of model. At the same time, Hopfield *et al.* (*J. Mol. Biol.*, **61**, 425; 1971) have been at pains to show that assorted rate data garnered from the literature are at no point inconsistent with an allosteric formulation. The oxygen saturation rate curves are adequately fitted in such terms, though not as well as by a set of Adair constants. Hopfield *et al.* regard such curve fitting as suspect, however, and insufficient evidence in favour of a model. Their own preference is based essentially on the ability of the allosteric formalism to absorb published data on the changes in concentration of rapidly reacting haemoglobin with the extent of ligand dissociation caused by flash photolysis.

At a more utilitarian level, and as a postscript to my account recently of the use of cyanate and related compounds to inhibit the sickling reaction in sickle cell anaemia, there is a new study by Gillette, Manning and Cerami (*Proc. US Nat. Acad. Sci.*, **68**, 2791; 1971). These workers, who were responsible for the original (and successful) attempt to mitigate sickling by reacting the chain termini of the abnormal haemoglobin with cyanate, have now examined the effect of such modification on the survival of the red cells in the patient. Cells, labelled with isotopic chromium, were treated with cyanate and then returned to their owner. The half-population survival time increased from an average of 10 to 21 days, which compares much more favourably with the 20–35 days survival span of normal cells. The latter were essentially unaffected by cyanate ion. This result then may turn out to be one of the occasional triumphs of the biochemist over a baleful phenomenon of nature.

Ribonuclease and Reverse Transcriptase

Few molecular biologists today would quarrel with the idea that infection of cells by RNA tumour viruses depends on the synthesis of a double stranded DNA molecule, the provirus, specified by the single stranded RNA genome, and that this synthesis is catalysed by reverse transcriptase. Baltimore and his colleagues have shown (*Nature New Biology*, **233**, 131; 1971) that reverse transcriptase is similar to DNA polymerase I of *Escherichia coli* and requires a primer with a 3′ hydroxyl group on which to initiate DNA synthesis, and countless groups have by now shown that an RNA/DNA hybrid molecule and some single stranded DNA molecules are intermediary to the appearance of double stranded DNA. Mölling and five colleagues working in Tübingen now report in next Wednesday's *Nature New Biology* the discovery of a ribonuclease activity, RNAase H, which seems to be responsible for the displacement of single stranded DNA from RNA/DNA hybrids.

Having recently isolated, from calf thymus cells, and RNAase which specifically digests the RNA strand of RNA/DNA hybrids, Mölling and his associates searched for a similar sort of activity in avian myeloblastosis virus particles (AMV) and sure enough they found it. Preparations of AMV particles disrupted with detergent will digest the RNA of RNA/DNA hybrids made either by transcribing calf thymus DNA with *E. coli* RNA polymerase or by annealing phage fd DNA with complementary RNA.

Mölling *et al.* then attempted to fractionate this RNAase H activity from the AMV virions but none of the several separation methods they used resulted in the separation of reverse transcriptase activity from RNAase H activity. Indeed the degradation of the single stranded RNA in the AMV particles by endogenous RNAase H was found to depend, at least in part, on the reverse transcription of this RNA. This discovery suggests that RNAase H activity is responsible for generating single stranded DNA during the synthesis of a provirus and it may well be that the polymerase and the ribonuclease activities reside in the same enzyme molecule. There is, of course, a precedent for this situation. DNA polymerase I of *E. coli* has both DNA polymerase and DNAase activities; the already considerable parallels between reverse transcriptase and DNA polymerase I may, therefore, extend still further.

Surface Characteristics of B Cells

Cellular immunologists are now devoting much effort to describing the heterogeneity of lymphocytes which, to the despair of the old-fashioned morphologist, look exactly alike. The efforts are directed partly to arrive at satisfactory counts of say B or T cells in various species, particularly man and, partly, to determine the functional attributes of lymphocytes. In next Wednesday's *Nature New Biology* two groups of immunologists, Fröland, Natvig and Berdal, and Dwyer, Mason, Warner and Mackay, report work which reflects these aims.

Fröland *et al.* have approached the problem of identifying B cells in man by the use of fluorescent anti-immunoglobulin antisera. Most theorists suppose that the capacity of B cells to be stimulated to antibody production depends initially on their possession of antibody-like receptors on the cell surface. Using a battery of more or less specific antisera conjugated with a fluorochrome marker, Fröland *et al.* found that up to 10 per cent of the peripheral blood lymphocytes from six normal patients showed visible fluorescence indicative of surface bound immunoglobulin. The monospecific antisera which were class or sub-class specific reacted with smaller percentages of cells. The marginal indication was that different cells carried different immunoglobulins on their surfaces. In contrast the blood lymphocytes from six patients with Bruton type agammaglobulinaemia, a complaint associated with failure to produce serum antibody, showed no staining with any antisera.

Wilson and Nossal using another technique (*Lancet*, ii, 788; 1971) have recently arrived at a figure of 34 per cent for the frequency of human lymphocytes with a high density of surface-bound immunoglobulin. The discrepancy between these results and those of Fröland *et al.* is probably indicative of a difference in sensitivity of the two techniques. But it is clear that with either method the surface-bound immunoglobulins are probably a sound characteristic of human B cells.

Dwyer *et al.* incubated spleen cells from nude mice, which are widely believed to be congenitally athymic, with a variety of different radioactively labelled antigens. They find that the proportions of labelled cells ($3-18\times10^{-4}$) were not significantly different between nude and normal mouse spleen cells, suggesting that only B cells are antigen binding cells (ABC as they say). In a sense this work dovetails nicely with the previous studies on immunoglobulins on the surfaces of B cells.

Roderick Murchison, Geologist and Promoter of Science

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Sir Roderick Impey Murchison (1792—1871) was a great stratigrapher who also made an impact on the British Association, the Geological Survey and the Royal Geographical Society.

SIR RODERICK MURCHISON died on October 22, 1871. He had taken up the study of geology as an amateur in 1824, largely by chance, at a time when the science was young and fashionable, and opportunities to attain distinction were wide open to any reasonably intelligent enthusiast who was fond of an open air life. This was particularly so for those who possessed sufficient private means to permit the devotion of their whole time to the subject, and this Murchison was able to do.

Roderick Murchison came from a west Highland family. He was the elder son of a doctor, Kenneth Murchison, who retired to a small estate at Tarradale in Easter Ross in the north of Scotland after making a fortune in India. Roderick Murchison was born here on February 19, 1792. He was educated at Durham Grammar School, and then entered the military school at Great Marlow. At the age of fifteen he received a commission in the 36th Regiment, and a year later saw active service in the Peninsular War, and was with Sir John Moore in the retreat to Corunna. After the defeat of Napoleon at Waterloo in 1815 it seemed to Murchison that prospects for further advancement in the army were small, and he retired with the rank of captain. He then married a lady of cultivated taste, and with her spent two years, chiefly in Italy, studying art and antiquities. At this time he acquired the habit of taking careful notes of all he saw, a practice that was to stand him in good stead later on in his geological work.

Murchison returned to England in 1818 and sold the family estate which he had inherited. He then settled, first in the north of England, and later at Melton Mowbray in Leicestershire. For the next few years he lived the life of a country gentleman, becoming one of the best known fox hunters in the Midlands.

A chance meeting with Sir Humphry Davy in 1823, at a partridge shoot, changed the whole course of Murchison's career. Davy suggested that he should take an interest in science and promised that he would soon get him into the Royal Society. The thought of giving up field sports would not have appealed to Murchison, but he concluded that if so distinguished a scientist as Davy could find time to indulge in them, then so could he; and so, encouraged by his wife, an amateur naturalist, he moved to London in 1824.

After arrival in London, on Davy's advice he attended W. T. Brande's lectures on chemistry and geology at the Royal Institution. He found that geology appealed to him particularly, so he began to study the subject seriously and became a member of the Geological Society of London. Soon he attracted the attention of some of the more prominent members of the Geological Society, notably William Buckland and Adam Sedgwick. In fact he seems to have very quickly impressed his personality not only on the members of this society, but on intellectual and social circles generally in London. Davy kept his promise, and in 1826 Murchison was elected a Fellow of the Royal Society not, obviously, on account of his scientific work, but because he was an independent gentleman having a taste for science, with plenty of time and money to gratify it. Such was the custom at that time.

Murchison was no dilettante, however, for he worked hard to make himself proficient in his new occupation, pursuing the study of geology with all the energy and enthusiasm he had formerly expended in the hunting field. He was fond of social activities, and these, no doubt, helped him in his career.

He soon became involved in the affairs of other organizations. In 1830 he became a founder member of the Royal Geographical Society and he was one of the earliest and most active promoters of the British Association for the Advancement of Science, which met for the first time in York in 1831. He took an active part in the affairs of both these societies for many years, but geology for long remained his principal interest. He was appointed a secretary of the Geological Society in 1826, elected president in 1831, and served on its council until almost the end of his life. For some thirty years after joining the society he devoted much of his life to geological field work. He travelled extensively in the summer months, both in Britain and over much of Europe, carrying out geological research and widening his knowledge. During these tours it was his habit to make the acquaintance of local geologists and absorb all the information he could from them.

One of his earliest journeys took him in 1826 to Brora in Sutherland, to examine its isolated coalfield, the age of which was at that time disputed. After a stop at York, he spent two days with the veteran English geologist William Smith, studying the Jurassic rocks of the Yorkshire coast. The information he gained from Smith helped him to establish the Jurassic age of the Brora coalfield, but he probably benefited even more from Smith's long experience of stratigraphical palaeontology. At all events, the two got on well together, and later on Murchison was one of those who supported an application to obtain a Civil List pension for Smith.

Stratigraphy

Stratigraphy was the branch of geology that appealed most to Murchison and it was as a stratigrapher that he made his name. About 1830 there was still one important gap in contemporary knowledge of the rock succession in Britain. Very little was known about the Lower Palaeozoic sediments below the Old Red Sandstone, apart from the facts that they occupied considerable areas and that they included some fossiliferous beds. They were called either "transition" beds, the name given to them by A. G. Werner, or simply "greywacke slates". Murchison's friend Sedgwick had started studying them in the Lake District and North Wales, but there was scope for investigation elsewhere. Murchison, on Buckland's advice, decided to examine the outcrops of these rocks in South Wales and the Welsh borderland.

Early in 1831 he set out, accompanied by "his wife and maid, two good grey nags and a little carriage, saddles being strapped behind for occasional equestrian use". This was the start of an investigation that lasted for several years. It resulted in the establishment, on the basis of fossil evidence, of an entirely new geological system, the Silurian System (much later to be divided into two systems, the Silurian and the Ordovician). The results were published in 1839 in Murchison's most famous book, *The Silurian System*, which was accompanied by a large geological map covering a large part of Wales and the adjoining parts of England. This was a major achievement, not only as far as British geology was concerned but for geology as a whole, for the silurian system was soon adopted by geologists throughout Europe and in America.

Murchison had been fortunate in undertaking the investigation of a series of rocks so little known. He extended his investigation of these rocks farther afield. It had come to his notice that in north-western Europe, particularly in Russia, there were vast areas of sedimentary rocks, undisturbed by Earth movements, which contained fossils similar to those found in the Silurian rocks in Britain. Murchison quickly seized the opportunity they offered, and in the summer of 1840 he set off for Russia to investigate them. He was accompanied by a French geologist, E. de Verneuil, a skilled palaeontologist. The journey, which lasted about three months, included regions in the neighbourhood of St Petersburg (Leningrad) and Moscow, and extended as far north as Archangel. This expedition was something of a preliminary canter, for Murchison was to visit Russia again; and canter is perhaps the right word, for he has described how the party rushed through the country in an open carriage drawn by five or six horses at a speed of ten to twelve miles an hour. Much of the country was in fact a flat drift covered plain in which exposures were few. Murchison, however, had the faculty of recognizing the salient geological features of a country quickly. During their tour the travellers proved the presence in northern Russia of a complete succession from the Silurian up to the Carboniferous, but Murchison brought back information of more immediate importance.

He and his companion had found beds containing fishes of Old Red Sandstone type interbedded with sediments containing marine fossils. This resolved beyond doubt a controversy in which he and other well-known British geologists had been engaged a few years earlier, the question of whether certain rocks in Devonshire containing marine fossils were coeval with sediments of Lower Old Red Sandstone age found in other parts of Britain. This discovery led to the establishment of another new geological system, the Devonian, the sandstones of the Lower Old Red Sandstone forming a continental facies of the system. Murchison was largely responsible for the establishment of this system.

Return to Russia

Murchison returned to Russia at the end of April 1841, again with de Verneuil, and this time a Russian geologist, Count A. von Keyserling, accompanied them. Through the British ambassador, Murchison made contact with Russian officials, and discussed his project with the Emperor of Russia. This was fortunate, for the expedition was greatly facilitated by official help and hospitality wherever it went; guides were particularly necessary, for detailed topographical maps were seldom available.

The area examined was extensive, including central and southern Russia and the Ural mountains. During this expedition the travellers outlined the stratigraphy and determined the broad general structure of the rocks in this area; they effected a general correlation with the sediments of western Europe.

Soon after his return Murchison announced that he had established, on stratigraphical and palaeontological evidence, yet another geological system overlying the Carboniferous and older than the Jurassic. This was the Permian, named after the Russian province in which it was best developed. It was soon realized that sediments well known in Germany, and also the Magnesian Limestone in the north of England, fitted into this system. The results of this Russian expedition were published by Murchison, de Verneuil and von Keyserling in 1845 in *The Geology of Russia in Europe and the Ural Mountains*. In 1856 Murchison, in collaboration with the Scottish geologist James Nicol, published a large geological map of Europe, on which the Silurian, Devonian and Permian rocks were differentiated.

Murchison had by now established for himself a European reputation, particularly for his work on the Palaeozoic rocks. His field work had not been confined to the Palaeozoic, however, for he had published important papers on other stratigraphic formations, and he continued to publish on British and continental geology for the next ten years. In 1854 his well-known book, *Siluria*, appeared, containing a wide ranging summary of all that was known about Silurian rocks at the time and discussions of cognate subjects. The fourth and last edition was published in 1867.

Geological Survey

In 1855 Murchison, the amateur, in effect turned professional. In his sixty-fourth year he was appointed to succeed Sir Henry de la Beche as Director-General of the Geological Survey and Museum, and of the Metropolitan School of Science applied to the Arts. The circumstances leading to this appointment were unusual. Concern had been expressed by members of the Geological Survey that a "most estimable man of a good family but possessing only a very slender acquaintance with geology" was likely to be appointed. As a result of a petition by eminent geologists outside the Survey the appointment was offered to Murchison. Changes were in the air, and it was planned (with the backing of the Prince Consort) to establish a great teaching establishment for science and technology at South Kensington. There was a possibility that the survey might lose its independence, and it was therefore a distinct advantage for it to have so influential a director. The appointment was a success, and he held it until his death some sixteen years later. One of his successors as director has said that "his eminence as a scientific man, his social position and wealth, his personal friendship with eminent politicians and members of the aristocracy, and his genial, forceful, assertive individuality made him an eminently successful director".

As a geologist, Murchison had his successes, but he also had his limitations, and he made mistakes. He was a keen-eyed and careful observer, with the power of marshalling facts, and he was a very hard worker. He lacked imagination, however, and his mind was not of the sort that evolves broad principles and new laws, but he was shrewd enough to know his own limitations and where his strength lay. His greatest success was as a stratigrapher, and in this field his work was of outstanding importance. On the other hand he was a strong opponent of the glacial theory introduced into this country in 1840 (though he was not alone in this); and he was sceptical of some of the new ideas about physical geology adopted during his lifetime. He refused to accept that the geological record lent any support to Darwin's theory, and Darwin, in a letter to Sir Charles Lyell, remarked: "How singular so great a geologist should have so unphilosophical a mind". Nor would he accept that the work of his old friend Adam Sedgwick on the Cambrian rocks established them as a separate geological system, and in his publications they were always treated as Lower Silurian. This disagreement led eventually to the estrangement of the two geologists.

Geologist and Geographer

Murchison's activities as a geologist had not prevented him from taking a prominent part in the affairs of the Royal Geographical Society, and during his later years he was probably more widely known for his connexion with this society than as a geologist. Though not a geographer in the modern sense, he had travelled widely, and he was very much in sympathy with the principal function of the society in the nineteenth century, the promotion of exploration in all parts of the world. In fact, his name has been perpetuated around the world in the naming of more than a dozen rivers, mountain ranges and so on. He served as president of the Royal Geographical Society for no less than seventeen annual terms, his final term of office extending from 1862 until his death. Features of the years in which he served as president were his anniversary addresses, which averaged 30,000 words in length and were all compiled by Murchison himself (though using contributions from other hands). They were delivered in abstract, but printed in full; and they provide a comprehensive review of the progress of geographical science and exploration during the first forty years of the society's existence. Apart from his public duties as president, Murchison did much behind the scenes to promote the affairs of the society. He was also largely responsible for the establishment of a separate section, E, for geography at the meetings of the British Association, and was first president of the section, at Ipswich in 1851.

Murchison had, in fact, taken a prominent part in the affairs of the British Association from its inception, particularly during the first ten or fifteen years of its existence, when not all scientists were in favour of its activities, and it was often ridiculed, especially by *The Times*. Murchison was president at the Southampton meeting in 1846. Referring to articles in *The Times* that year he protested against their "ribald vulgarity and ignorance", saying that he was ashamed that his "eminent foreign friends should go away with the impression that *The Times* in its vituperation of science represented my country". Murchison was a trustee of the British Association from 1832 to 1870 and a general secretary from 1836 to 1845.

He seems to have played a less prominent part in the affairs of the Royal Society, though he was one of those who opposed the election of the Duke of Sussex as president in 1830, on the grounds that a scientific man was preferable. The duke was elected by a small majority, and being a wise man, chose to select his council from those who had opposed him, for they chiefly represented science in the society. Murchison, being among those chosen, "deemed it his duty to accept office under a prince who could act so liberally and kindly towards his opponents". He received the society's Copley Medal in 1849 for his services to geological science, in particular for his work in establishing the Silurian System.

As a promoter of science there is no doubt that Murchison played an effective part. He worked very hard, for many years, on behalf of the several societies to which he belonged; and possibly of equal value were his activities in publicizing science, through the British Association and by other means. He and his wife held prominent positions in London society, and his wealth permitted him to entertain lavishly. The receptions held at his house in Belgrave Square were attended by both scientists and prominent politicians. Thus, Murchison was able to exercise very considerable influence in official circles whenever he thought it desirable to do so in the interest of science as a whole, or even of individual scientists. His considerable wealth also enabled him to support and encourage the advance of science. Just before he died he persuaded the government to found a chair in geology in Edinburgh University, and contributed £6,000 towards its endowment. Previously geology had been taught by the professors of natural history, and the Murchison chair in geology was the first separate chair in the subject in any Scottish university. In his will Murchison left £1,000 each to the Geological Society and the Royal Geographical Society, for the promotion of geology and geography respectively, and his name is perpetuated by the annual award of a Murchison Medal by the former society. He is also known to have exercised his influence in all manner of ways to help on individuals in lowly walks of life, particularly if they were interested in science.

Although Murchison had his failings, they were far outweighed by his achievements. He was, in his time, one of the great leaders of science, and his personality gained for scientists as a class greater recognition and respect from society at large.

The Bacterial Cell Surface

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This article deals with some of the foci of activity and current problems in the complex and multidisciplinary field of bacterial cell surface studies.

In 1965 Bayer and Anderson[1] published an artistic reproduction of what they could see on the surface of negatively stained *E. coli*. In 1971 the secrets of the "mountains" and "craters" of that lunar landscape are still very much with us and hold fascination for an increasing number of scientists. Thin sections or freeze fractured images of bacteria allow one to make out the multilayered three dimensional structure of the bacterial surface[2-4]. As a result of careful comparative work with the methods of cytology and biochemistry it is now possible to assign at least a rough chemical composition and biological function to these surface layers[5,6]. The innermost trilaminar structure adhering to the cytoplasm is the plasma membrane. It contains most of the cellular lipids, as well as protein and carbohydrate, and it forms the main permeability barrier of the cell. It is this structure that is most comparable with the plasma membrane of eukaryotic cells. In some rare instances, in bacteria living in unusual habitats, such as some halophylic bacteria or bacterial L-forms[7], the plasma membrane is the only surface layer of the cells. In the great majority of bacteria, however, there are several additional surface layers exterior to the plasma membrane. The first one of these is a layer of varying thickness made up mainly of an extensive network of glycopeptide units: the bacterial peptidoglycan. In spite of some species to species variability in chemical composition, the basic structure of these glycopeptides is remarkably similar throughout the bacterial world: glycan strands made up of a polymer of a disaccharide and an attached network of cross-linked peptides. This bacterial surface component seems responsible for the defined shape and mechanical stability of the cells and most of the effective antibacterial agents as well as viruses cause disintegration of bacterial cells by damaging the peptidoglycan (through inhibition of a biosynthetic step or through enzymic dissolution). Glycopeptides and glycoproteins are, of course, ubiquitous throughout the living world, but the bacterial glycopeptide is unique in its size and shape: it covers the entire surface of the bacterium by what seems to be a continuous, covalently interlinked network of glycopeptide units which on isolation and purification still retain the characteristic shape of the particular bacterium[8,9].

In Gram positive bacteria, attached to the peptidoglycan and probably on the outer surface of it, one can find a variety of complex polysaccharides, polyolphosphates or "teichoic acids". These are major antigenic components and can also form the receptors for several bacteriophages. In Gram negative bacteria on the exterior of a thin peptidoglycan layer one can see another trilaminar structure, indistinguishable in dimensions from the plasma membrane. This is the "outer membrane", containing lipopolysaccharide (LPS), lipid and protein material. The great variety of *E. coli* and *Salmonella* serotypes reflect the chemical variability of this LPS structure[10,11]. Bacteria with deficient LPS are non-virulent in their vertebrate hosts and therefore it seems that in the absence of homologous antibody the LPS serve as a protective coating against destruction by host phagocytes and serum. Of course, once encountered by the vertebrate host, the protection offered by the particular LPS is annulled by the production of specific antibodies. The immunochemistry of LPS structure is a fascinating record of a continuing evolutionary "chess game" between the bacterium and its vertebrate host: every mutational twist and change in the molecular structure of LPS is matched and counteracted by the production of appropriate antibodies. The outer membrane also contains receptors for specific extracellular macromolecules (for example, colicines) and viruses.

Very little is known about the architectural principles, that is, the bonds (covalent, ionic or others) which hold the various macromolecular units of a single surface layer together, and even less is known about how the various surface layers are anchored to one another and to the cell. A very interesting protein which seems to perform the role of such a structural anchor has been described recently. It forms covalent bridges between the ε-amino group of lysine residues in the peptidoglycan and some lipoprotein component of the outer membrane[12].

Specialized Areas of the Surface

In addition to its heterogeneity in depth the bacterial surface also shows distinct horizontal differentiation. Electron microscopic studies of *E. coli* have shown that several hundred points of adhesion between the plasma membrane and the outer layer persist even during extensive plasmolysis. The functional importance of these areas was made clear by the observation that in live bacteria they represent the exclusive areas of attachment for a number of phages, such as T2, T4, T6, φX174 and λ[13]. It should be remembered that several of these viruses have distinct receptor sites. This finding indicates that clusters of different virus receptors are organized into several hundred distinct topographic areas of the surface.

In order to understand how the combination of binding proteins with their substrates leads to the oriented chemotactic[14] movement of flagella (and the whole cell) it is necessary to understand their fine structure, their mode of insertion into the surface and their spatial relationship to the binding proteins. Progress in such a work was described recently[15].

"Periplasmic" enzymes have now been localized at the cellular tips[16]. In *E. coli* a number of specific enzymes (mostly hydrolytic) and binding proteins (implied in chemotaxis and transport) can be released in controlled quantities from *E. coli* by an osmotic shock procedure, in the absence of cell death and without release of a large number of typical intramembrane components.

In many bacteria there is a complete reorientation of surface growth at the site of cell division in the form of septa which move inward to divide the bacterium into two daughter cells of the same genetic and chemical composition, size and shape[17]. The cellular control of both the site of initiation and the rate of growth of septa is a central problem in cell division. Biochemical analysis of this problem is just beginning now, following the isolation of a wide variety of genetic mutants and physiological variants in which various abnormalities of septum formation can be observed[18-23].

In streptococci the first observable sign of cell division is the appearance of a local thickening or "notch" in the cell wall at the cellular equator. Next, one can observe the splitting of the notch into two halves, which proceed to move, one to the left, the other to the right of the equator, while the septum grows inward. By the time compartmentalization of the cell is complete the two notches will have reached the exact midpoint between the tips of the parent cell and the completed septum, that is, they are aligned at the sites of the next cell division. Independent evidence indicates that this bilateral movement of cell wall is propelled by the incorporation of new surface elements at or inside the septum while the "old" hemispheres of the surface are conserved and moved to the left and to the right. These findings reveal an asymmetry of the cell surface: half of the surface (including the original tips of the parent) is one generation older than the other half (which includes the area proximal to the septum of the parent) and the cell wall notches mark the boundary between the two[24].

Towards a Functional Anatomy

Not only do the surface lamellae serve as structural components (the only ones that a bacterium has) but built into these layers are the molecular units which determine the specificity of interaction between the bacterium and the thousands of molecules bombarding it from the environment. Whether or not a molecule would be absorbed and transported inside the cell boundaries, or a substance recognized as a chemotactic stimulant, depends on the presence of specific proteins on the surface. The "gates" for the entry of transforming DNA molecules, sites for contact with a virus, a colicine molecule, a hostile Bdellovibrio or a friendly bacterium of opposite sexual polarity, survival or destruction by vertebrate macrophages—in short, the entire "social" life of bacteria—depend on the cellular surface.

Which molecular elements of the surface mosaic are responsible for these ectobiological functions? One of the main current activities of the field is to find answers to this question. This involves localization of the various biological activities to the various surface layers as well as attempts to characterize functional units biochemically. It is now becoming possible to solubilize selectively the surface layers into anatomically relevant fractions, that is, into components that correspond to elements recognizable by electron microscopy[25-28].

Well over sixty specific proteins have so far been localized in the plasma membrane. This includes transport carriers: membrane vesicles prepared from a number of bacteria can carry out energy-driven, specific intravesicle transport of as many as twenty substrate molecules[29]. Proteins of the electron transport chain, the phosphotransferase II enzymes[30], and enzymes catalysing the biosynthesis of membrane lipids[31], peptidoglycan[32,33], teichoic acid[34,35] and lipopolysaccharide (M. J. Osborn, personal communication) are all localized in the plasma membrane. Many of these enzymes have peculiar physical properties, which distinguish them from cytoplasmic enzymes. Some require lipid cofactors, others are soluble in aqueous solvents only in the presence of detergents. The C_{55} isoprenoid alcohol phosphokinase of *Staphylococcus* is completely insoluble in hydrophilic solvents, but can be extracted into butanol. This enzyme purified to homogeneity shows an unusually high content (58%) of nonpolar amino-acids (highest of all proteins as yet isolated[36]).

The narrow host range of complex biological agents, such as bacteriophages, colicines (extracellular inhibitory macromolecules) or competence factors (agents inducing the ability to absorb DNA from the environment), is based on the presence of surface receptors in the sensitive cells. The solubilization of such receptors has been reported in several instances. Once detached from the bacterium, the recognition of such activities is usually based on a neutralization assay: inactivation of the virus or colicine and so on by soluble fractions prepared from the sensitive (but not from the resistant) bacteria. Fractionation of colicine K receptor[37] and solubilization of colicine E3 receptor were reported[38]. The two activities are distinct and both are located in the outer membrane of *E. coli*. In bacteriophage T4 the lipopolysaccharide receptor seems to react with the part of the tail fibres containing antigens B and C[39]. Protein-like receptors for two competence factors were localized in the plasma membrane[40,41].

The making of the structural heteropolysaccharides of bacteria is quite different in several respects from the synthesis of cytoplasmic polysaccharides, for instance, glycogen: (*a*) the assembly of the macromolecules occurs in distinct stages which correspond to different intracellular localization;

(*b*) during some of these stages the biosynthetic intermediates are covalently attached to lipid carrier molecules; (*c*) some of the synthetic steps involve unusual mechanisms.

The first, cytoplasmic stage of peptidoglycan synthesis corresponds to the stepwise synthesis of the two parts of the eventual glycopeptide: part one is UDP-N-acetyl muramic acid with the pentapeptide (L-Ala-D-Glu-L-Lys or DAP-D-Ala-D-Ala) side chains already attached; part two is UDP-N-acetyl glucosamine. The second stage of biosynthesis takes place in or on the plasma membrane. Part one of the glycopeptide is transferred from UDP to a lipid carrier molecule, a C_{55} isoprenoid alcohol phosphate and all the subsequent steps of assembly occur with the reducing group of muramic acid attached (in pyrophosphate bond) to the lipid, called glycosyl carrier lipid (GCL)[42]. These subsequent steps include formation of the disaccharido–peptide (through linking up with the N-acetylglucosamine) and modification of the peptide side chain. These latter involve the attachment of short oligopeptide chains (composed of alanine, glycine or threonine) to the free amino group of the lysine or DAP residue of the disaccharido–peptide. The peculiarity of this reaction is that the amino-acid donor seems to be aminoacyl-transfer RNA, functioning in the apparent absence of ribosomes or mRNA[43]. The third stage of this synthetic sequence is transport of the GCL-linked and modified disaccharido–peptide units (or, possibly, their oligomers) to some acceptor sites in the peptidoglycan layer of the surface. The final stage is incorporation into the old surface. Practically nothing is known about the mechanisms of transport. The only definite information we have about the mechanism of incorporation is that the glycopeptide units are added in covalent linkage to some acceptor sites (possibly through glycosidic bonds with the carbon atom 4 of some terminal glucosamine residue) in the old peptidoglycan network. A second and last reaction at present known is cross linking (by peptide bonds) of the peptide side chains of neighbouring glycopeptide units. The existence of cell wall growth zones in some bacteria (see later) suggests that the active acceptor sites of the peptidoglycan may also be clustered at the equatorial zone of the cell surface.

In LPS synthesis, the molecule is also made in two parts: the "core" region and the O-antigenic chains[44]. The early (cytoplasmic?) stages of the synthesis of the former are not well understood, and in the case of the O-antigen the very first synthetic step already occurs in or on the plasma membrane. This is the transfer of galactose from UDP-gal to a GCL, an isoprenoid alcohol phosphate which seems chemically identical to the one functioning in peptidoglycan synthesis. All the subsequent reactions, the build-up of the trisaccharide, their polymerization and eventual linkage to the other half ("core") of the LPS, occur by membrane-bound enzymes and with the oligosaccharide chain attached to GCL.

The other part of *Salmonella* LPS, the so-called "core" region, is synthesized by stepwise transfer of sugar residues from UDP-linked precursors to the growing end of the oligosaccharide which also contains covalently bound lipid (the so-called lipid A). Each step is catalysed by a specific enzyme and the first indication that the core was made in a lipid membrane came from the discovery of a peculiar phospholipid requirement: the oligosaccharide would only accept a new sugar residue in the presence of a glycerophosphatide, containing unsaturated or cyclopropane fatty acids and a certain type of polar group. More specifically, the acceptor had to be "annealed" with the phospholipid by heating. On adding the appropriate enzyme protein to the lipid and oligosaccharide a ternary complex of these could be isolated by sucrose density gradient centrifugation.

These experiments were recently repeated in an *in vitro* monolayer system in order to approximate the *in vivo* conditions[45]. A mixed monolayer film was constructed stepwise: acceptor oligosaccharide molecules were allowed to penetrate a film of phosphatidylethanolamine; next, the enzyme molecules were introduced in a similar fashion and finally radioactive UDP-sugar was introduced in the subphase of the tricomponent film. Several striking observations were made. (1) In the monolayer, "annealing" of the acceptor and the P-lipid was no longer necessary for the attachment of a sugar residue. (2) While in the reaction occurring in suspension several hundred sugar units would incorporate per enzyme molecule, in the monolayer only about two. (3) Monolayers which were prepared with phospholipids inactive in the suspension assay were found inpenetrable by the polysaccharide acceptor molecules.

Recent work in Osborn's laboratory (personal communication) has demonstrated that all the biosynthetic enzymes for the synthesis of both the "core" region and the O-antigenic chains of LPS are located in the "inner" (plasma) membrane. Pulse chase experiments showed that the biosynthesis of LPS molecules is completed in the plasma membrane and these molecules are then transported to the outer membrane apparently without the GCL. Nothing is known about the mechanism of transport.

Incorporation into the Cell Surface

The "anchoring" of various macromolecules into the appropriate pre-existing surface layer occurs by various types of lateral interactions with components of the "old" surface and we know very little in biochemical terms about these. The monolayer studies on LPS synthesis provided some suggestions concerning the types of lateral interactions which may also occur *in vivo* between lipid, polysaccharide and protein molecules sharing a common surface layer. One of these suggestions is the structural requirement in the lipid component for successful mixed film formation. The restriction of the activity of surface-bound enzyme leads to the proposal[44] that the synthesis of the core polysaccharide *in vivo* may occur by the diffusion of the incomplete polysaccharide through a properly arranged cluster of enzymes, each adding one sugar unit to the substrate. This would, of course, be reminiscent of other organelle-linked biosyntheses, such as ribosomal protein synthesis. Nothing is known about the organization of the components of outer membrane in the well-membrane junctions[13], which must include clusters of virus receptor LPS molecules.

In the growth of the plasma membrane the various functional protein molecules cannot be arranged completely at random either, for proper functioning of some of these requires that they be in the close vicinity of one another. This must be, for example, the case with D-lactic dehydrogenase and transport proteins which derive energy from lactose oxidation[46]. Clearly we cannot even start thinking in biochemical terms about how the topographic arrangement of specific proteins is brought about in such differentiated areas of the surface as flagella or periplasm.

There are numerous examples for specific interactions between lipids and proteins also during incorporation into the plasma membrane. While functional proteins (as well as bulk protein) can apparently incorporate into the membrane in the absence of lipid synthesis[47], such proteins may function inefficiently[48,49]. In some cases this inefficiency can be corrected for by subsequent resumption of lipid synthesis[49]. In the case of some membrane proteins at least, the newly made proteins tend to associate with lipid made at the same time. A fatty acid auxotroph of *E. coli* growing on oleic acid was briefly shifted to linoleic acid and induced for β-galactoside transport. On returning to the oleic acid medium, the galactoside transport rate of such cells at different temperatures was typical of linoleic-acid grown cells. Consistent results were found in the reverse experiment or if the same culture was induced for two independent transport systems. In each case, the properties of the permease indicated that some time during incorporation into the membrane newly made protein preferentially associated with lipid incorporated at the same time[50]. Whether the peculiar (hychophobic) properties of membrane-bound enzymes always appear *in statu nascendi*, or whether they may acquire these in some post ribosomal event, perhaps by interaction with lipids in the membrane, is not known. In fact it is not even known if such membrane-bound enzymes are functional prior to incorporation into the membrane. Some of these proteins may be present in an inactive zymogen form while in the cytoplasm, similar to the case of several secretory enzymes in eukaryotic cells.

The mode of surface extension in the macroscopic sense has been approached by several experiments. In biochemical terms practically nothing is known about mechanisms of this process, thus the more biological term "growth" seems adequate. All the more appropriate is this term, since the problems of biosynthesis at this level merge with such fundamental cell biological problems as the control of cell division, mechanism of chromosome segregation and control of cellular morphology.

Experiments were designed to ask two separate but interrelated questions. (i) What is the size of the parental surface that is conserved during cellular growth and division? (ii) Do new components enter the pre-existing surface at random locations or within localized growth zones? The first question was approached in segregation experiments in which a specific surface component of the parent cell was labelled (with isotope or fluorescent antibody) and subsequently the distribution pattern of the label was determined among progeny cells by quantitative autoradiography or fluorescence microscopy. The first experiment of this sort was done in *E. coli* labelled with ^{3}H-DAP[51]. From six to eight generations of segregation the distribution of radioactivity in the progeny cells was random, implying that the parental peptidoglycan was broken up and passed on to progeny cells in no less than about 250 fragments. In a similar experiment with *E. coli* segregation of lipid label was followed. A distinct deviation from a random (Poisson) distribution of the label was observed between the sixth and eighth progeny generation[52]. This finding implies that the lipid containing parental surface layer (plasma membrane and/or outer membrane?) may be broken up to no more than about 250 units (a surface area of about 5×10^{4} nm^{2}) which would then be conserved during subsequent growth.

A variation of the experimental design in such studies exploits chain formation of bacteria: the labelled parental cell is put under conditions which allow cell division but prevent physical separation of daughter cells. The resulting "chain" of bacteria represents a linear clone with progeny cells lined up in a nice geometric arrangement. From the localization of label within such "chains" one can deduce the pattern of segregation[53].

In the Gram positive bacterium *Streptococcus pyogenes*, Cole and Hahn[54] and May[55] were first to demonstrate by an immunofluorescence technique the conservation of surface antigens (polysaccharide?) during growth. These experiments were reproduced in several other Gram positive bacteria[56] also and were confirmed by an autoradiographic method in the case of teichoic acid or pneumococcus[57].

Growth Zones

The simplest interpretation of a non-conservative segregation is that growth of the surface occurs at many points, while in conservative segregation growth may be restricted to one or few zones. While consistent with such interpretations, segregation experiments cannot prove zonal or multiple site growth. To answer this second problem requires different techniques. Direct evidence for the existence of growth zones was obtained in the case of streptococcal surface antigens (presumably polysaccharide)[56], M-protein[58], capsular polysaccharide and the choline containing teichoic acid of pneumococcus[60], by immunofluorescence or electron microscopic methods. It is interesting that a number of chemically distinct macromolecular cell components occupying different strata in the surface structure all enter the cell surface at the same equatorial growth zone.

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Network Thermodynamics

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The techniques of network theory are generalized to include irreversible thermodynamic systems. Complex nonlinear systems can be treated in this way in terms of a well-defined mathematical structure.

CLASSICAL thermodynamics is limited in that it deals only with the initial and final equilibrium states of a process; it provides no information about the dynamical behaviour between these states. Thermodynamics tells us where we have been and where we are, but not how we got there.

Nonequilibrium thermodynamics, as developed by Onsager and others[1-4], has been successful in correlating many physical, chemical and biological phenomena. It falls short of a complete dynamical theory, however, because it treats only the irreversible aspects of processes and is thus an algebraic theory restricted primarily to describing time-independent (steady) states. Moreover, the stringent restriction of linearity is placed on the admissible constitutive relations between the thermodynamic forces and fluxes, thus excluding many nonlinear phenomena which seem to dominate the dynamical behaviour of biological systems. Another serious limitation of the Onsager formalism is the difficulty of providing a macroscopic description when a system is complex; yet inhomogeneity and anisotropy are the hallmarks of organizational complexity in biological systems. In this article we attempt to resolve some of these difficulties by combining classical and irreversible thermodynamics with modern network theory.

Network Theory

Thermodynamics is a phenomenological theory and, as such, is a purely formal structure. It offers no "explanation" of physical events, but serves only to organize knowledge and establish relationships between quantities. Similarly, the principal purpose of the phenomenological theory proposed here is to provide an organizational framework for treating complex thermodynamic processes. The techniques developed here are especially well suited to the description of biological systems, where analysis is complicated by the nonlinearity of the individual dynamic processes, the organizational complexity of the system as a whole and the mathematical intractability of the resulting equations.

These problems are similar to those encountered in dynamical systems and control theory, where one particular application of nonequilibrium thermodynamics—electrical network theory—has been extremely successful. Circuit analysis is not usually considered as an application of nonequilibrium thermodynamics, no doubt because its specialized techniques seem quite foreign to the classical methods of thermodynamics. In fact, however, the network approach is quite general, and with modifications it can be applied widely to thermodynamic systems (see ref. 5). Indeed, the network approach to irreversible processes has several advantages. Not only does it provide a formalism, but it brings thermodynamics within the framework of modern dynamical systems theory, thus bringing to bear a great body of analytical tools on the problem of biological complexity. The technique described here is not, however, merely an alternative version of "equivalent circuit" modelling; rather, the objective is to exploit the underlying unity in the mathematical description of all dynamical theories[6].

The network approach also makes it possible to construct a graphical representation for thermodynamic systems analogous to circuit diagrams in electrical network theory. Such network graphs are far more than pictorial representations of particular physical systems. Because the dynamical equations may be read algorithmically from the network graph, the diagrams are actually another notation for the equations themselves in much the same way as the operators of vector analysis are a more lucid notation for the component representation. In addition the network graph actually contains information not available in the bare differential equations—it reveals the system topology. This crucial aspect has been largely neglected in the treatment of thermodynamic systems. Yet the way in which a system is "hooked up" will impose a set of constraints on its behaviour which endow the system with its organizational character: a system of capacitors, resistors, and so on functions as a radio only if they are appropriately connected.

Underlying the network approach is the duality of the mathematical structures available for the description of dynamical systems: point set topology and algebraic or combinatorial topology. Continuum theories use vector calculus, whose operational structure arises from point set topology, to generate partial differential field equations. Combinatorial topology, on the other hand, describes the continuum by examining it at a finite number of specified points, giving rise to ordinary differential equations. Both point set topology and its discrete counterpart, algebraic topology, seek to describe the connectivity properties of the space in which the dynamical processes are described. In the network approach we "pull apart" the continuum, revealing the implicit topological relations. For example, if we wish to describe the current and potential distribution on a conducting sheet, instead of trying to specify the entire distribution by continuous functions we could overlay the sheet with a network or mesh of a finite number of nodes and branches and tabulate the meter readings giving the current flow through each branch and the potential differences between each node pair. It seems reasonable that, as the mesh is made finer and finer, we can approach the actual continuum distribution to any desired degree of accuracy. In fact, in the limit of infinitesimal mesh size, the linear operators, represented by the connexion matrices of the network, become the differential operators of vector calculus[7,8]. In this spirit, Kron and others have constructed network representations for practically all of the field equations of physics, from the Navier-Stokes equations to Schrödinger's equation[9-14], and the technique has also been used to represent certain aspects of membrane function[15,16].

The general plan of this development of network thermodynamics involves three steps. First, constructing an isomorphism between the thermodynamic system and a topological or graphical structure. Second, imposing upon this graphical structure an algebraic or analytical structure equivalent to the equations of thermodynamics. Third, exhibiting the computing algorithm generated from the graphical representation.

State Variables and Constitutive Relations

The central device employed in network thermodynamics is the conceptual separation of "reversible" and "irreversible" processes. That is, we mentally reticulate the system into subsystems, each of which either stores energy reversibly or dissipates energy without storage[17]. Furthermore, we suppose that each subsystem or element is characterized by a finite number of ports, that is, interactions with its surroundings. Elements are frequently classified by their number of ports. (In circuit theory a 1-port is sometimes called a "2-terminal device"[26].) In addition, we define ideal energy bonds which are generalizations of perfectly conducting wires, infinitely stiff rods and other ideal "connectors" which transmit power instantaneously and without loss or storage from one element to another. For electrical circuits, these idealizations assume a concrete form: ideal capacitors and resistors are separate 1-port (2-terminal) physical devices. The separation of reversible and irreversible processes in, for example, a chemical reaction is, however, a purely mathematical device.

Before dealing with the first step we must define the dynamical variables used for the description of the system. Equilibrium thermodynamics postulates that there exists a unique state function, the internal energy $U(S,V,N_k,\ldots)\equiv U(q_1,q_2,\ldots,q_n)$, which is a function of the various thermodynamic displacements q_i such as the entropy S, the volume V, and the number of moles of the kth component N_k. Taking the differential of U and defining the conjugate potentials—temperature T, pressure p and chemical potentials μ_i—one obtains the Gibbs equation

$$\mathrm{d}U = \sum_{i=1}^{n} \frac{\partial U}{\partial q_i}\,\mathrm{d}q_i \equiv T\mathrm{d}S - p\mathrm{d}V + \Sigma\,\mu_i\,\mathrm{d}N_i \qquad (1)$$

Rather than attempting to obtain a dynamical theory from an equilibrium relation by dividing by dt, it makes more sense to go the other way: to start with a dynamical theory and require that it reduce to the correct equilibrium theory.

Most systems that can be analysed with the network approach share one common property: the rate of energy transmission, dissipation or storage is finite and may be expressed as a product of an "effort" or force variable, e, and a flow variable, f; that is, energy rate (power)$=e{\cdot}f$. In electrical networks these variables are, of course, voltage difference and current; in mechanics: force and velocity; in diffusional processes: chemical potential difference and mass flow; in chemical reaction: affinity and rate of reaction; and so on.

By integrating e and f we can define two additional state variables: the generalized displacement,

$$q\,(t) \equiv q\,(0) + \int_0^t f\,(t)\,\mathrm{d}t \qquad (2)$$

and a generalized momentum,

$$p\,(t) \equiv p\,(0) + \int_0^t e\,(t)\,\mathrm{d}t \qquad (3)$$

For example, ξ, the advancement of a chemical reaction, is a generalized displacement variable, defined here by equation (2) as

$$\xi\,(t) = \xi\,(0) + \int_0^t J_r\,\mathrm{d}t$$

where J_r—the reaction rate—is the flow variable.

As in electrical network theory, we associate two dynamical variables with each energy bond: a variable (f or q) which obeys a local conservation law (Kirchhoff's current law, KCL), and a variable (e or p) which is a continuous function (Kirchhoff's voltage law, KVL). The latter property is related to the local equilibrium postulate[18].

In order to make predictions based on any phenomenological theory, information must be supplied about the system in the form of constitutive relations (equations of state, branch relations). These are obtained either experimentally or from a more detailed theory, such as statistical mechanics.

There are three kinds of energetic transactions possible: that is, three ways of integrating the equation $P=\mathbf{e}{\cdot}\mathbf{f} = \sum_{\text{ports}} e_i f_i$.

$$E_C\,(t) = \int_0^t \mathbf{e}{\cdot}\mathbf{f}\,\mathrm{d}t = \int_{\mathbf{q}(0)}^{\mathbf{q}(t)} \mathbf{e}.\,\mathrm{d}\mathbf{q} \qquad (4)$$

to give capacitative, or "displacement" energy storage,

$$E_L\,(t) = \int_0^t \mathbf{f}{\cdot}\mathbf{e}\,\mathrm{d}t = \int_{p(0)}^{p(t)} \mathbf{f}.\,\mathrm{d}\mathbf{p} \qquad (5)$$

to give inductive, or kinetic energy storage, and

$$E_R\,(t) = \int_0^t \mathbf{e}{\cdot}\mathbf{f}\,\mathrm{d}t \qquad (6)$$

to give energy dissipation.

To perform the first integration we require capacitive constitutive relations between the displacement and charge variables of the form

$$\mathbf{q} = \Psi_c\,(\mathbf{e}) \qquad (7)$$

An ideal multiport element, which stores energy by virtue of a generalized displacement, will be called a capacitor, and denoted generically by C. (In instances of biological interest such a device may be a volume element which stores chemical energy due to a thermodynamic displacement.) From the constitutive relation (7) we obtain

$$\frac{\mathrm{d}\mathbf{q}}{\mathrm{d}t} = \frac{\mathrm{d}\Psi_c}{\mathrm{d}\mathbf{e}}\,\frac{\mathrm{d}\mathbf{e}}{\mathrm{d}t} \qquad (8)$$

Defining the reversible flow on the capacitor:

$$\mathbf{f}_{\text{rev.}} \equiv \frac{\mathrm{d}\mathbf{q}}{\mathrm{d}t}$$

and the incremental capacitance

$$C \equiv \frac{\mathrm{d}\Psi_c}{\mathrm{d}\mathbf{e}} \qquad (9)$$

we obtain:

$$\mathbf{f}_{\text{rev.}} = C\frac{\mathrm{d}\mathbf{e}}{\mathrm{d}t} \qquad (10)$$

where **e** is the unique potential characterizing the capacitor. To illustrate this generalized notion of a capacitor we can consider the case of an ideal mixture for which the chemical potential of the ith component is $\mu_i = \mu^0{}_i + RT\ln X_i$, where X_i is the mole fraction, μ_i is the chemical potential and $\mu^0{}_i$ the reference potential of the ith component. By equation (9) the incremental capacitance is

$$C_i = \left(\frac{\partial N_i}{\partial \mu_i}\right)_{P,T,n_j} = \frac{N_i}{RT(1-X_i)} \approx \frac{N_i}{RT} \text{ for } X_i \ll 1 \qquad (11)$$

where N_i, the number of moles of species i, is the displacement variable q and the effort, e, is $\mu_i - \mu_i{}^0$.

Energy may also be stored as a result of the relative motion of mass or charge (that is, kinetic or electromagnetic energy). In such cases, the second integration can be performed, given the constitutive relation $\mathbf{p} = \Psi_L(\mathbf{f})$. This type of energy storage device will be denoted by L, a generalized inductance. In mechanical networks the constitutive relation between momentum and velocity is merely the mass[19-21].

Finally, for the dissipative element, denoted by R, we require the constitutive relation between e and f in order to compute the energy dissipation. For example, in a chemical reaction the effort, conjugate to the reaction flow, J_r, is the chemical affinity, A, which is related to J_r by the constitutive relation

$$A = \Psi_R(J_r) \qquad (12)$$

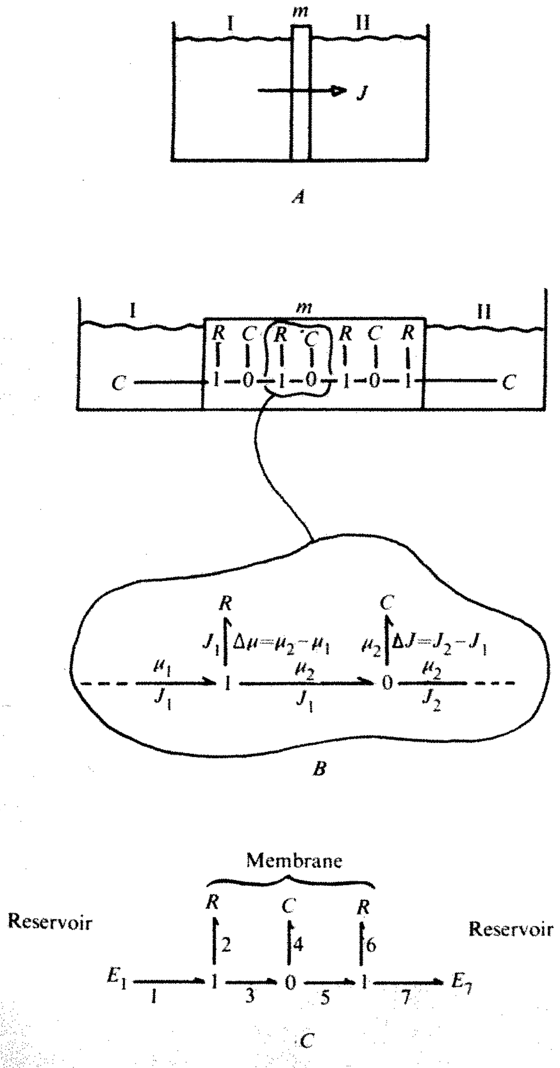


Fig. 1 Diffusion bond graph.

The incremental resistance R of a chemical process is

$$R \equiv \frac{\partial A}{\partial J_r} = \frac{\partial \Psi_R}{\partial J_r} \qquad (13)$$

It is worth noting that as a chemical reaction proceeds, the free energy dissipated by the reaction is the difference between the free energy supplied by the reversible discharging of the local capacitors of the reactants and the free energy stored by the charging of the product capacitors.

As another example of the separation of reversible and irreversible processes, consider the case of membrane transport (Fig. 1*A*). A complete description of the system must include not only the dissipative processes but also the reversible discharge of permeant from compartment I, its concomitant reversible accumulation in compartment II and the concentration changes within the membrane itself. The latter aspect is central when analysing nonsteady transport across the membrane: for it is only in a steady state that the concentration in the membrane is time independent and the process may be treated as a pure irreversible phenomenon. On the other hand, during the course of a nonsteady flow, the membrane may gain or lose permeant so that the capacitance of the membrane itself must be considered.

The ideal elements (R, L, C)—plus one additional device to be introduced later—are sufficient to construct finite dimensional representations of most thermodynamic systems. Note that the letters R, L and C are only symbolic notations for the constitutive relations themselves. The existence of such functions is equivalent to the postulate of local thermodynamic equilibrium on which the validity of nonequilibrium thermodynamics rests. Moreover, we take as our definition of reversible and irreversible the existence of unique port constitutive relations (L, C) and (R), respectively. Fig. 2 shows the relation of the state variables to the constitutive relations.

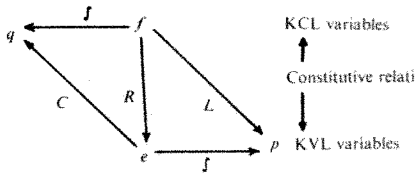


Fig. 2 State variables and constitutive relations.

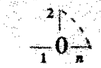
Bond Graphs

The representation of dynamical systems other than electrical networks by linear graphs is a well established technique in engineering[19-21]. They quickly become unwieldy, however, and confusing for even moderately complex systems. In order to represent more general processes, in which many types of energy are involved, a more satisfactory graphical notation called bond graphs has been developed. This notation, devised by H. Paynter (see refs. 22–25), is particularly well suited for nonequilibrium thermodynamics. This generalization of linear graphs treats all energetic flows on an equal footing and hence provides an easily visualized notation for energy conversions and coupling.

In bond graphs we introduce a set of junctions that generalize the notion of series and parallel connexions, and that permit us to join the ports of the energy processing elements. These junctions may be considered as black boxes consisting only of connexions (connexion n-ports[26]). Mathematically, these are simply a graphical notation for the set of linear constraint equations (KCL) and (KVL).

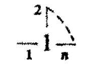
We require these junctions to be ideal in the sense that they neither store nor dissipate power: $\Sigma e_i f_i = 0$, where the sum is over all energy bonds incident on the junction.

First, a parallel or zero-junction, denoted by 0-junction:



is defined by $e_1 = e_2 = \ldots = e_n$, or, since $\Sigma e_i f_i = 0$; $\Sigma f_i = 0$.

Second, a series or one-junction, denoted by 1-junction:



and defined by $f_1 = f_2 = \ldots = f_n$, or since $\Sigma e_i f_i = 0$; $\Sigma e_i = 0$.

Note that each junction contains a statement of KCL (conservation), KVL (continuity) and conservation of energy, any two implying the third. A 0-junction may be regarded as a distribution point for flows; that is, flows split when incident on a 0-junction. Conversely, the effort splits or distributes when incident on a 1-junction. The one and zero-junctions lump together all flows and efforts that are equal.

To illustrate how a bond graph is constructed, consider the simple case of a single permeant diffusing through a homogeneous membrane (see Fig. 1*A* and refs. 24, 28). We assign capacitances to the membrane as well as to the reservoirs to allow for reversible charging and discharging of the permeant. Because dissipation accompanies each flow process, a resistive element must be assigned at both the entrance and exit of each volume element. The larger the number of volume elements considered, then the closer the ordinary differential equations will be to the continuum behaviour. By definition, there is a drop in chemical potential across the dissipative element, but no accumulation of permeant. Similarly, to each capacitative element we assign a unique chemical potential, and the flow must split in passing through the element since part of the flow goes for reversible charging. These conditions are fulfilled by inserting 1 and 0-junctions as shown in Fig. 1*B*. A consistent sign convention is the following: First, assume a positive power-flow direction; say from left to right as in Fig. 1*B*. This is indicated by appending a half-arrow to the energy bonds. Second, take power as positive into each element, so that, for example,

$$\rightharpoonup R \quad e = \Psi_R(f)$$
$$\leftharpoondown R \quad e = \Psi_R(-f)$$

As a simple example of how the bond graph generates the governing state equations algorithmically, consider the relaxation time of a one-lump membrane. We will assume that the bounding compartments are so large that they may be effectively time independent, that is, an infinite capacitance is equivalent to a constant effort source, which we denote by E (Fig. 1*C*). For illustrative purposes all the constitutive relations are assumed to be linear. The constitutive relation for the membrane capacitor is therefore $C_4 e_4 = q_4$. Then

$$C_4 \frac{\mathrm{d}}{\mathrm{d}t} e_4 = \frac{\mathrm{d}}{\mathrm{d}t} q_4 \equiv (f_4)_{\text{rev.}} \qquad (14)$$

According to the definition of a 0-junction $f_4 = f_3 - f_5$ while the 1-junctions imply that $f_3 = f_2$ and $f_5 = f_6$. The constitutive relation between dissipative flow and effort leads to $f_2 = e_2 / R_2$ and $f_6 = e_6 / R_6$, so that

$$C_4 \frac{\mathrm{d}}{\mathrm{d}t} e_4 = \frac{e_2}{R_2} - \frac{e_6}{R_6} \qquad (15)$$

Again, according to the definition of the 1-junctions $e_2 = E_1 - e_3$ and $e_6 = e_5 - E_7$. Further noting that, for a homogeneous membrane, $R_2 = R_6$ are the membrane resistance R_m and C_4 is the membrane capacity C_m, we obtain:

$$\frac{\mathrm{d}e_4}{\mathrm{d}t} = \frac{1}{R_m C_m} [(E_1 - e_3) - (e_5 - E_7)] \qquad (16)$$

Reverting to thermodynamic notation and identifying E_1 and E_7 with the chemical potentials μ^{I} and μ^{II} of the reservoirs, we may define

$$\langle \mu \rangle \equiv \frac{E_1 + E_7}{2} = \frac{\mu^{\text{I}} + \mu^{\text{II}}}{2} \qquad (17)$$

where $\langle \mu \rangle$ is the average chemical potential in the containers. Further, since $e_3 = e_4 = e_5 = \mu_m$, the chemical potential of the permeant in the membrane, the last equation leads to the relaxation expression

$$\frac{\mathrm{d}\mu_m}{\mathrm{d}t} = \frac{2}{R_m C_m} [\langle \mu \rangle - \mu_m] \equiv \frac{\langle \mu \rangle - \mu_m}{\tau_m} \qquad (18)$$

The relaxation time for the membrane process

$$\tau_m = \frac{R_m C_m}{2} \qquad (19)$$

has the expected form of an RC time constant familiar from network theory. The magnitude of R_m evaluated for an ideal permeation process is

$$R_m = \frac{RT\Delta x}{D_m (N_i / V)}$$

where D_m is the diffusion coefficient within the membrane and Δx the membrane thickness. The volume V is here the volume of the membrane per unit area or $V = \Delta x \cdot 1\ \text{cm}^2$, and hence the ideal membrane capacity according to equation (11) is

$$C_m = \frac{(N_i / V)\, \Delta x}{RT}$$

Inserting the magnitudes of R_m and C_m into equation (19) we regain the Einstein equation

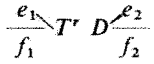
$$\tau_m = \frac{(\Delta x)^2}{2 D_m} \qquad (20)$$

Since R is experimentally determined at steady state while C is obtained at equilibrium, only equilibrium and steady state measurements are required to characterize the dynamic behaviour of systems in network thermodynamics.

The important point here is that the dynamical equations, linear or nonlinear, for arbitrarily complex systems, are generated algorithmically from the bond graph. Therefore it is a simple matter to design a computer program that will accept the bond graph as its input and then compute the dynamical behaviour directly from the graph without dealing with the differential equations explicitly. In most cases the complexity of the system precludes analytical solutions in any event, so that it is easier to deal directly with the more intuitive graphical representation.

Coupled Phenomena

In order to treat energetic coupling and conversion in irreversible processes, we introduce an additional ideal element: a 2-port device that acts as an ideal converter or transducer. We denote it by:



and define it by the equations:

$$\begin{bmatrix} e_1 \\ f_1 \end{bmatrix} = \begin{bmatrix} r & 0 \\ 0 & -1/r \end{bmatrix} \begin{bmatrix} e_2 \\ f_2 \end{bmatrix} \text{ or } \begin{array}{l} e_1 = r\, e_2 \\ f_1 = -1/r\, f_2 \end{array} \qquad (21)$$

We see from the defining equation that the ideal transducer has two properties: first, it neither stores nor dissipates energy; viewed as a mapping from input space, (e_1, f_1), to output space

(e_2, f_2), $e_1 f_1 + e_2 f_2 = 0$. Second, it is a reciprocal device since its constitutive relation is a symmetric matrix.

The factor r is called the transducer modulus and includes the conversion units from the energy form on side 1 to the energy form on side 2. The modulus r may also be a function of other state variables in the system, and in this fashion we may incorporate pure signal flows and parametric feedback into thermodynamics[24,25]. The transducer (TD) generalizes the notion of the ideal lever and transformer familiar from elementary physics. It is merely a pictorial representation of a set of constraint equations (and units conversion) on e and f, analogous to the 0 and 1-junctions.

To illustrate the use of the transducer to represent thermodynamic coupling let us consider the coupled diffusion of substances A and B passing a membrane. It is assumed that the two species interact according to the following requirements. First, their coupling is dissipative, and second the coupling interaction depends on the relative motion of the two species.

The coupling structure shown in Fig. 3*A* is easily seen to fulfil these requirements; it is represented by the coupling resistance R_c and also by the 0-junction. The diffusing species clearly must be coupled through the 1-junction, because the energy exchange between the species occurs only during flow. As shown elsewhere[25], this bond graph reproduces the equations corresponding to the usual frictional model of diffusion coupling[29-31].

An alternative coupling between the diffusional flows of A and B is through a chemical reaction in which, for example, substance A is converted into substance B.

Here the transducer element TD is employed again, not for the representation of pure energy conversion, but for the stoichiometric conversion of a species in a chemical process. The flow of a chemical reaction J_r is

$$f \equiv J_r = \frac{1}{\nu_i}\frac{dN_i}{dt} \text{ by KCL} \qquad (22)$$

and the associated effort is the affinity

$$e \equiv A = -\Sigma\, \nu_i\, \mu_i \text{ by KVL} \qquad (23)$$

where ν_i = stoichiometric coefficient of species i.

Let us now allow the diffusing species in the previous example to react chemically with one another as they migrate across the membrane: $\nu_A A \rightleftharpoons \nu_B B$. We must couple the local capacitors of species A and B through a reaction 2-port. The reticulation of this 2-port for near equilibrium reactions is shown in Fig. 3*B*. The reticulation for reactions far from equilibrium requires a profound modification, dealt with in ref. 25. It is easy to see from the definitions of each element that the structure shown corresponds exactly to the correct thermodynamic equations for a chemical reaction. A reaction is always accompanied by dissipation, accounted for in the constitutive relation of R_r, which in general is nonlinear. The expression for the affinity can be written in the form of KVL: $A + \Sigma \nu_i \mu_i = 0$, which defines the 1-junction of the reaction 2-port. The moduli of the transducers are then the stoichiometric coefficients.

A straightforward calculation verifies that the bond graph algorithm produces a finite difference equivalent of the diffusion-reaction field equations[24,25]. Moreover, the bond graph allows a clear topological separation of the reversible and irreversible processes accompanying a chemical reaction. The reversible part clearly must be present in reaction as well as in diffusion, in order to treat non-stationary behaviour.

The network technique described above has been used by us to describe several experimental systems. These include diffusion-reaction studies, including facilitated and active transport, rectification properties of complex membranes and relaxation oscillations in coupled membrane systems[25,32]. In all cases good agreement between the bond graph solution and the experimental results was obtained.

Once the network representation for thermodynamics has been established, a large body of theory becomes available, permitting many previous results to be viewed from a unified perspective. One of the central unifying conclusions in network theory is Tellegen's theorem[33]. It is remarkable that virtually every energy distribution theorem for thermodynamic networks as well as several results from nonequilibrium thermodynamics may be derived starting from this powerful theorem[34,35]. The reason for its generality is that it is a purely topological result, based only on KCL and KVL, and is independent of any assumptions concerning either the constitutive relations or stationality. Since 1883, when Heaviside first used a form of Tellegen's theorem to derive Maxwell's minimum heat theorem (minimum entropy production), versions of the theorem have reappeared in various forms from time to time in the engineering and mathematics literature. However, the first to recognize and exploit its generality and usefulness was B. D. H. Tellegen[33]. For an account of its historical development and references to continuum versions and applications of Tellegen's theorem, see ref. 35. Here we restrict ourselves to a brief heuristic discussion of this fundamental theorem from a thermodynamic viewpoint.

Network thermodynamics, like electrical network theory, considers only systems in which the sources of interest (reservoirs) are included in the system. The sources are regarded as system elements which interact with the rest of the system

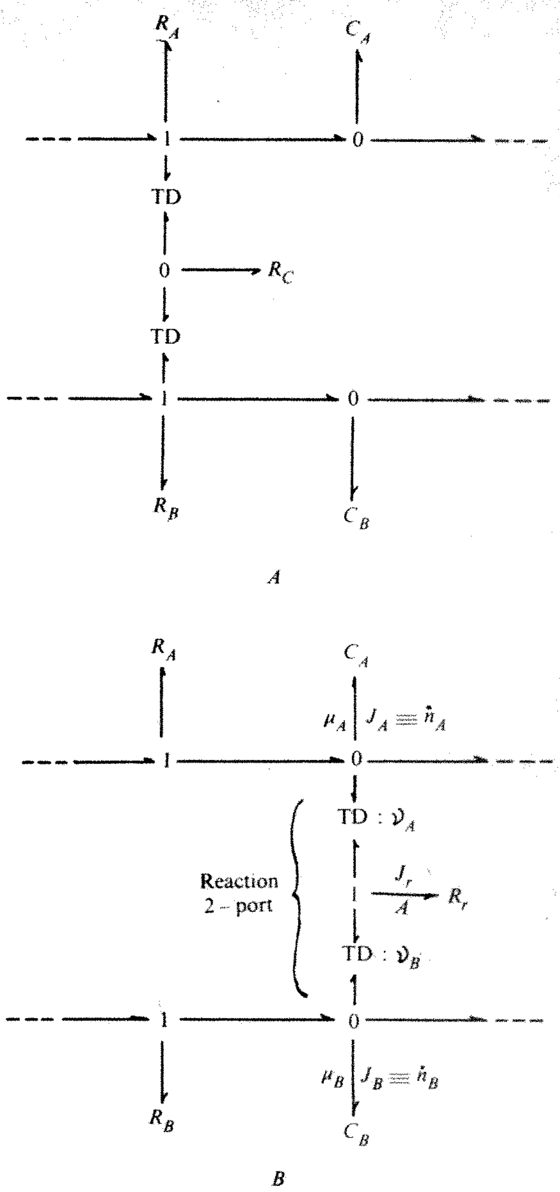


Fig. 3 *A*, Diffusion coupling; *B*, reaction coupling.

through specified ports. Thus, in the membrane example, the compartments adjacent to the membrane were considered as an integral part of the system. The systems considered here are therefore closed and may be assumed isothermal and isobaric. In accord with the requirements of the second law of thermodynamics, the free energy of the system, G, as determined in the capacitative elements, is found to decrease with time, or

$$\frac{\mathrm{d}G}{\mathrm{d}t} < 0 \tag{24}$$

This decrease is attributed to the dissipative processes and indeed dissipation is identified with $-\mathrm{d}G/\mathrm{d}t$. An adequate measure of irreversibility is the dissipation function

$$\varphi \equiv T\frac{\mathrm{d}_i S}{\mathrm{d}t} > 0 \tag{25}$$

where $\mathrm{d}_i S/\mathrm{d}t$ is the positive definite entropy production. From a classical point of view we may say that the energy dissipated by all irreversible processes proceeding in a closed, isothermal and isobaric system is equal to the decrease in free energy, that is,

$$\frac{\mathrm{d}G}{\mathrm{d}t} + \varphi = 0 \tag{26}$$

Equation (26) may be cast in the suggestive form

$$\varphi + \frac{\mathrm{d}G}{\mathrm{d}t} = \sum_{\text{irrev.}} e_i f_i + \sum_{\text{rev.}} e_j f_j = 0 \tag{27}$$

which is the thermodynamic form of Tellegen's theorem. Equation (27) may be given a striking geometrical interpretation by defining two state vectors

$$\begin{aligned} \mathbf{f} &\equiv (\underbrace{f_i, \ldots, f_m}_{\text{irrev.}};\ \underbrace{f_{m+1}, \ldots, f_n}_{\text{rev.}}) \\ \mathbf{e} &\equiv (\underbrace{e_i, \ldots, e_m}_{\text{irrev.}};\ \underbrace{e_{m+1}, \ldots, e_n}_{\text{rev.}}) \end{aligned} \tag{28}$$

Therefore,

$$\mathbf{e}\cdot\mathbf{f} = 0 \tag{29}$$

The scalar product of $\mathbf{e}$ and $\mathbf{f}$ is equivalent to equation (27), and hence equation (29) may be interpreted as an orthogonality condition between the flow and effort state vectors. That is, the 2n dimensional state space defined by all the efforts and flows is decomposed into the direct product of two orthogonal subspaces. No assumptions of linearity or steady state are required; the orthogonality condition holds at each instant of time regardless of the nature of the system[7,33,35].

Reciprocity and Onsager's Relations

In nonequilibrium thermodynamics, if linear constitutive relations are assumed, reciprocity appears as the symmetry of the matrix relating the various forces and fluxes. In this context it is usually called Onsager reciprocity. More generally, if the port quantities are related by a nonlinear function

$$\mathbf{e} = R(\mathbf{f}) \tag{30}$$

reciprocity is the symmetry of the Jacobian of R:

$$\mathrm{J}_R = \mathrm{J}_R^{\mathrm{T}} \tag{31}$$

where $\mathrm{J}_R^{\mathrm{T}}$ is the transpose of matrix $\mathrm{J}_R = (\partial e_i/\partial f_j)$.

Mathematically, reciprocity is merely an integrability condition on the constitutive relations, assuring the existence of a unique real valued function of the port parameters, which, when differentiated, yields all the constitutive relations. In equilibrium thermodynamics, the existence of such a state function is postulated—it is the internal energy or its Legendre transforms and the resulting reciprocity conditions are the well known Maxwell relations. Physically, reciprocity of a system assures us that if we vary the input on one energetic port while observing the effect at another port, we may then reverse the position of input and observer and expect to obtain symmetrical measurements—at least up to small signal. That is, there exists a unique scalar function which is able to account for variations in all the port parameters.

For thermodynamic systems represented by bond graphs consisting of reciprocal elements, reciprocity is assured due to a theorem proved by Brayton[26] which states that any interconnexion of reciprocal elements—that is, elements characterized by a symmetrical Jacobian matrix of constitutive relations—is reciprocal. Note that each 1-port is trivially reciprocal, since its Jacobian is just a number. Moreover, it can be shown that "connexion n-ports (junctions) are also reciprocal[26]. The proof of the overall reciprocity of the system employs only Tellegen's theorem and the topological statements of conservation (KCL) and continuity (KVL) that have been imposed on the system by definition[24,27].

It is important to note that the extended definition of reciprocity given here includes both reversible and irreversible processes, and is valid when the functional relationship between forces and flows is nonlinear. A system composed of reciprocal components will exhibit only "trivial" dynamic behaviour, that is, monotonic decay to a stationary point. Oscillations and amplification are not possible with reciprocal systems. Hence biological systems are generally not reciprocal.

State Equations

For finite dimensional dynamical systems the equations of motion are usually given in the state space form: $\dot{\boldsymbol{\chi}} = \boldsymbol{F}(\boldsymbol{\chi}, \boldsymbol{\alpha})$; where $\boldsymbol{\chi}(t)$ describes the trajectory in state space and $\boldsymbol{F}$ is the vector field propelling the state point. It is of paramount importance in dynamical theories to have a general prescription for the vector field $\boldsymbol{F}$. For instance, in classical mechanics, the canonical equations of Hamilton describing the evolution of any conservative mechanical system have the form:

$$\mathcal{J}\,\boldsymbol{\chi} = \nabla\mathbf{H} \tag{32}$$

where

$$\mathcal{J} = \begin{bmatrix} \mathbf{O} & \mathbf{I} \\ -\mathbf{I} & \mathbf{O} \end{bmatrix},\quad \boldsymbol{\chi} = \begin{bmatrix} \mathbf{q} \\ \mathbf{p} \end{bmatrix},\quad \nabla\mathbf{H} = \begin{bmatrix} \partial H/\partial\mathbf{q} \\ \partial H/\partial\mathbf{p} \end{bmatrix}$$

For a wide class of nonlinear reciprocal networks, the Brayton–Moser equations[24] have an equally elegant form:

$$\mathcal{J}\dot{\boldsymbol{\chi}} = \nabla\mathcal{P} \tag{33}$$

Where $\mathcal{J}$ is a metric obtained from the reversible elements,

$$\mathcal{J}_{ij} = -\Sigma L_{ij}(\mathbf{f})\mathrm{d}f_i\mathrm{d}f_j + \Sigma C_{ij}(\mathbf{e})\mathrm{d}e_i\mathrm{d}e_j$$

and $\mathcal{P}$ is a mixed potential obtained from the irreversible constitutive relations. The differential equations obtained earlier for the transient membrane diffusion are a simple example of these equations. For nonreciprocal dissipative systems, the state equations are not a gradient flow, and the Brayton–Moser–Smale equations take the form[25]:

$$\mathcal{J}\dot{\boldsymbol{\chi}} = \boldsymbol{\omega} \tag{34}$$

where $\boldsymbol{\omega}$ is a nonintegrable differential form.

A large class of irreversible thermodynamic systems are described by these equations, and hopefully they will prove as valuable for thermodynamic systems as Hamilton's equations have been for point particle mechanics.

The techniques of network theory have been generalized to include a large class of irreversible thermodynamic systems. This approach has several advantages. First, it is capable of treating nonlinear, nonsteady systems of great complexity that include coupling and feedback effects. Second, an intuitive graphical representation is available. Third, a computing algorithm is generated enabling the equations of motion to be read directly from the graph. Finally, a well-defined mathematical structure emerges, paralleling the modern axiomatic development of dynamical systems and network theory, which proves a unified perspective and generalization of previous results in nonequilibrium thermodynamics.

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Rotating Relativistic Ring

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Consideration of a rotating ring sheds light upon the problem of the rotating disk recently discussed in *Nature* by several authors and shows the disk problem to be more difficult than it appears.

THERE has recently been appearing in *Nature* an interesting correspondence about the relativistic treatment of a rotating disk[1–6]. As the writers recall, the problem goes at least as far back as 1909 when Ehrenfest formulated a paradox on the inference that at any place in the disk lengths in the direction of motion would suffer the FitzGerald–Lorentz contraction while lengths perpendicular to this would be unaffected by the motion. This inference is incorrect, but the reason seems not to have been stated explicitly in the correspondence.

The problem is of peculiar interest, in the context of the discussion, only for the case of what may be called a "rigid" disk. In relativity theory, however, no disturbance may be propagated through matter with more than the speed of light c. Consequently in relativity theory there cannot exist anything like a classical rigid body, in which all disturbances are propagated instantaneously. Of course, were it possible to have a body in which all disturbances are propagated with speed c, it would be natural to regard this as the analogue of the classical rigid body and to proceed accordingly. Actually, however, it appears to be impossible to select a self-consistent set of elastic constants so that even all infinitesimal disturbances, compressional, transverse and torsional, travel with speed c. In fact, there is as yet no satisfactory relativistic treatment of a two dimensional or three dimensional "rigid" body. Probably there are, indeed, many possible choices depending on the kind of disturbance for which the speed of travel is to be maximized. In this situation, it is clear that the problem of the rotating "rigid" disk is very far indeed from having yet been solved.

The solution of even the problem of a rotating "rigid" ring seems not to have yet been given. However, this may be treated as an application of the theory of the relativistically rigid rod, which Hogarth and McCrea[7] (HM) gave many years ago. In this article I seek to solve the ring problem, and I consider briefly also the problem of the rotating rigid rod. In the light of this work, I then discuss the problem (but not its solution!) of the rotating disk.

As previous authors have remarked, since gravitation is not involved, only special relativity is concerned.

Rigid Ring

In HM we discussed a uniform straight "rod" that has the maximum degree of longitudinal rigidity permitted by relativity theory. We treated it as a one dimensional body and, as we remarked, nothing corresponding to flexural rigidity makes its appearance in one dimensional problems. So I may now suppose the ends of the rod to be joined so as to make it into a ring.

The intrinsic properties of the material, which I shall call the wire, are then the same as before. When the wire is at rest in an inertial frame under tension T, let L be the length and m the mass per unit length, and let L_0, m_0 be the values when $T=0$. From HM (3.1), (3.2) we have

$$T = \tfrac{1}{2} m_0 c^2 [1 - (L_0/L)^2], \quad m = \tfrac{1}{2} m_0 [1 + (L_0/L)^2] \qquad (1)$$

Ring in Rotation

Let S be an inertial frame and let the wire be in a plane fixed in S; let the wire be in a state of steady rotation such that it forms a circle with centre O, fixed in the plane, and with radius a, and such that every particle of the wire is moving with speed V along the circle. We may think of the ring as moving in contact with a fixed smooth plane over a fixed circle drawn on the plane. This circle may be graduated in a scale of length; standard clocks synchronized in S in the standard fashion may be situated along the circle. Any particle P of the moving ring may be marked, so that its velocity in S may be observed. If such a particle also carries a standard clock, we postulate that this clock measures proper time in the history of P. This is the usual "clock hypothesis" in the usual formulation of special relativity. If, when the moving clock is passing a fixed clock that reads zero, it also reads zero, then when it is passing a fixed clock that reads t, the moving clock reads $\beta^{-1}t$ where $\beta=(1-V^2/c^2)^{-1/2}$. This follows at once by calculating the interval along the world-line of P between the two events.

Let $l=2\pi a$ be the length of the wire, measured in S; it is by definition the length of the fixed circle along which the whole length of the wire lies at any given instant in S. Then the proper-length of the wire L is

$$L=\beta l \qquad (2)$$

This follows directly from the FitzGerald–Lorentz contraction, or by calculating the orthogonal interval between the world-lines of two neighbouring particles of the wire, or by considering light-travel times measured by an observer moving with a particle like P (see later).

In HM the relativistic equation of motion (4.2) in the inertial frame concerned states

$$\beta^2(m-T/c^2)\times \text{acceleration} = \text{force per unit length} \qquad (3)$$

The only factor that may be unexpected is $m-T/c^2$, rather than simply m; HM remarked that its correctness was checked by the fact that the equation gives c for the speed of wave propagation for all values of T. In the present case, the acceleration is V^2/a towards O and the force per unit length on any element of the wire is T/a as can be seen by resolving the tensions at the two ends of the element along the radius through its midpoint. Then (3) gives

$$(1-V^2/c^2)^{-1}(m-T/c^2)V^2=T \qquad (4)$$

Using (1), (2) we then find from (4)

$$T=(1+V^2/c^2)^{-1}V^2 m_0 \qquad (5)$$

$$m=(1+V^2/c^2)^{-1}m_0 \qquad (6)$$

$$L=(1+V^2/c^2)^{1/2}(1-V^2/c^2)^{-1/2}L_0 \qquad (7)$$

$$mL=(1-V^4/c^4)^{-1/2}m_0 L_0 \qquad (8)$$

$$l=(1+V^2/c^2)^{1/2}L_0 \qquad (9)$$

Thus $a=(1+V^2/c^2)^{1/2}A_0$ where A_0 is the radius of the ring at rest.

Check on First Approximation

Before interpreting the foregoing results, it is instructive to obtain a first approximation by elementary methods. In HM we note that for small extension the wire obeys Hooke's law with modulus λ where $\lambda=m_0c^2$, which it must do if small disturbances are propagated along it with speed c. So we now suppose that $V\ll c^2$ in which case we may use this approximation. We find directly from classical mechanics $T\approx m_0V^2$. So the proper length of the wire is by Hooke's law

$$L=(1+T/\lambda)L_0\approx(1+V^2/c^2)L_0 \qquad (10)$$

To the same order (2) gives

$$l\approx(1-\tfrac{1}{2}V^2/c^2)L \qquad (11)$$

Combining (10), (11) again to the same order

$$l\approx(1+\tfrac{1}{2}V^2/c^2)L_0 \qquad (12)$$

It is seen that these very elementary results agree with those of the previous section to order V^2/c^2.

Interpretation

Equation (12) shows from elementary mechanics that the most rigid possible ring allowed by relativity theory must be seen to expand when set in rotation relative to an inertial frame. From (9), the precise expansion factor is $(1+V^2/c^2)^{1/2}$.

As V increases from zero to c, the radius increases from A_0 to $\sqrt{2}A_0$.

Once we see that the radius must begin to increase when the ring is set in rotation, we can see that the result found is qualitatively the only one that it is reasonable to expect. For if the radius begins to increase it is only natural to suppose that it will not decrease again as it is caused to rotate still faster. So as $V\to c$ the radius must tend to a finite limit greater than A_0 or must tend to infinity. But it would make no sense mechanically for an originally finite ring to be spun out to an infinite extension at a zero angular velocity!

The other features also are what we might expect on general grounds. As $V\to c$ the proper-length tends to infinity, and T,m tend to the corresponding limiting values.

The old argument was that an inextensible ring would, by definition, retain its proper-length and so would actually shrink to a smaller radius when set in motion. On the face of it, this seems absurd; we see that it is absurd because there can be no such thing as an inextensible ring.

At the same time, it might seem that some of the factors containing V appear somewhat "artificial". However, we have to appreciate that the case of rotation is quite artificial so far as rigidity properties are concerned, and so we have no cause to expect particularly elegant formulae. The one thing we ought to expect is that if we have two rigid rings of the same radius, we should not be able to make them more or less rigid by joining them together. This is borne out by the absence of m from the formulae for L and l.

Rotating Rigid Rod

Let us now suppose that our original rigid rod is rotating about one end fixed at O in the frame S; suppose that it moves in a plane and that it is "straight" in a suitably defined sense; let ω be its (uniform) angular velocity in S. If P is any particle of the rod, let $OP=r$ where $r=r_0$ when $\omega=0$. Since every part of the rod moves at right angles to itself in S, we may treat r as a distance in S and also as proper-distance along the rod. Thus the speed of P in S is $v=r\omega$. For given ω the distance $r=r(r_0)$ is a function of r_0 only, such that $r(0)=0$. As before, let L_0 be the undisturbed length of the rod, and let $L=r(L_0)$ be its length when rotating; we write $V=L\omega$ for the tip-speed of the rod.

In this case m, T are functions of r, and in place of (1) we now have

$$T(r)=\tfrac{1}{2}m_0c^2[1-(\mathrm{d}r_0/\mathrm{d}r)^2],\ m(r)=\tfrac{1}{2}m_0[1+(\mathrm{d}r_0/\mathrm{d}r)^2] \tag{13}$$

and as a boundary condition we require $T(L)=0$. The equation of motion (3) now becomes

$$\beta^2(m-T/c^2)r\omega^2=-\mathrm{d}T/\mathrm{d}r \tag{14}$$

where $\beta=(1-v^2/c^2)^{-1/2}$. Using (13), this gives a second order differential equation for $r(r_0)$. Solving it in accordance with the boundary conditions and using the solution in (13), it is found that

$$\omega r/c=\sin[(\omega r_0/c)(1-\omega^2L^2/c^2)^{-1/2}] \tag{15}$$

whence, in particular, putting $r_0=L_0$,

$$\omega L_0/c=(1-V^2/c^2)^{1/2}\sin^{-1}(V/c) \tag{16}$$

$$T=\frac{1}{2}m_0\frac{(L^2-r^2)\omega^2}{1-r^2\omega^2/c^2} \tag{17}$$

$$m=m_0\frac{1-\frac{1}{2}(L^2+r^2)\omega^2/c^2}{1-r^2\omega^2/c^2} \tag{18}$$

These results may be verified by direct substitution in (13), (14).

As before, we may also check these to the first order in v^2/c^2 by classical mechanics applied to a uniform rod having modulus $\lambda=m_0c^2$. Elementary classical treatment yields

$$\omega r/c=\sin(\omega r_0/c)\sec(\omega L_0/c)$$

$$\omega L/c=\tan(\omega L_0/c)$$

$$T=m_0c^2[\cos(\omega r_0/c)\sec(\omega L_0/c)-1]$$

$$m=m_0\cos(\omega L_0/c)\sec(\omega r_0/c)$$

If $\omega L_0 \ll c$, these give to order v^2/c^2

$$r\approx r_0[1+\tfrac{1}{2}(L_0^2-\tfrac{1}{3}r_0^2)\omega^2/c^2] \tag{19}$$

$$L\approx L_0(1+\tfrac{1}{3}\omega^2L_0^2/c^2)\approx L_0(1+\tfrac{1}{3}V^2/c^2) \tag{20}$$

$$T\approx\tfrac{1}{2}m_0(L_0^2-r_0^2)\omega^2 \tag{21}$$

$$m\approx m_0[1-\tfrac{1}{2}(L_0^2-r_0^2)\omega^2/c^2] \tag{22}$$

It is clear that equations (15)–(18) give the same results to this order.

At the other extreme we see from (16) that as $V\rightarrow c$ we have $L\rightarrow\infty$ and $\omega\rightarrow 0$; also from (17), (18) $T\rightarrow\frac{1}{2}m_0c^2$, $m\rightarrow\frac{1}{2}m_0$ in agreement with (1) when $L\rightarrow\infty$.

If (16) be regarded as an equation for ω as a function of V, or as a function of L, then it is found that ω has a maximum for a particular value of V between 0 and c, and for a particular value of L between 0 and infinity, and ω tends to zero at the ends of the interval. For any intermediate value of ω there are two possible values of V and of L. All this behaviour is plausible on general grounds. As regards infinite extension in S, the difference between the cases of the rotating ring and the rotating rod is due to the fact that in S the ring is everywhere moving along its length whereas the rod is everywhere moving at right angles to its length. Thus, in particular, the ring can have infinite proper-length but finite relative length when its speed tends to c while the rod must have infinite length but zero angular speed in the limit when its tip-speed tends to c.

Discussion

Comparing (9), (16) it is seen that for given V the resulting values of l/L_0 and of L/L_0 are quite different, and from (12), (20) it is seen that they are different even to the first order in V^2/c^2. If a rigid wheel is made of a rigid circular ring with rigid rods as spokes, then when it rotates the rim and the spokes will react on each other, so they cannot behave precisely as we have calculated for the cases in which they rotate independently. That is at any rate the way in which they will tend to behave, however. Thus the rim and the spokes tend to change their lengths in different ratios, whence it is to be inferred that the wheel cannot remain circular. This seems to be the nearest we can get at present to solving the problem of the rotating disk.

There are further considerations that render the problem more complicated than it might appear even after noting the difficulties already mentioned. One is that, while axial symmetry is naturally specially significant in regard to rotation, the case of a disk of uniform thickness is no more special than that of a disk whose thickness depends on the radial distance r. For, as we see from a relation like (18) in the case of a uniform rod, uniformity is in any event lost as a result of the rotation itself. Thus there is no uniquely significant problem of "the" rotating disk.

Another complication concerns the means of setting a system in motion and the state that may be treated as one of steady rotation. This cannot be investigated here. But the simple cases of steady motion of the ring and the rod do appear to be perfectly possible physically. On the other hand, the motion considered, for example, by Weinstein[6], whatever its significance, is not a state of steady motion.

Here it may be remarked that another interesting problem that has not yet been solved, but whose solution would be highly instructive, is that of an infinitely long rotating "rigid" circular cylinder.

Inertial Frames

The chief value of the sort of problem here considered is that it exhibits the significance of inertial frames in relativity theory. An inertial frame in special relativity is a freely moving, non-rotating, rigid body. In such a frame a rigid measuring rod has its usually assumed properties. Special relativity deals only with such frames because they are the only physically possible "frames" allowed by the theory. This is for the simple physical reason that the theory cannot admit undeformable bodies. If an accelerated observer tries to use a rigid measuring rod, the behaviour of the rod would be hopelessly confusing; it would depend on the point of the rod at which it is held as well as on what had been happening to the rod beforehand.

On the other hand, if a problem can be solved using any inertial frame, then it is possible to say what an accelerated observer will observe. For the behaviour of the required light-signals may be worked out using the inertial frame; in particular, the proper-times of arrival and departure of signals at the observer can be calculated. Provided the observer may be assumed to carry the "proper-clock" previously mentioned, the results are observable by him.

As opposed to this, observable results cannot in general be obtained by means of coordinate transformations. In particular, the "rotating coordinates" discussed in the correspondence referred to cannot have any direct physical meaning. It is essential to appreciate that this is a consequence of the basic physical restriction that matter cannot transmit effects with speed greater than c. The difficulty is not produced by any limitation—physical or mathematical—of special relativity as such. In fact the situation is exactly the same in general relativity except that, if a true gravitational field is present, then any inertial frame has only a local significance.

All this has to do with the principles of the theory. In practical applications, the classical notion of a rigid body is normally an adequate approximation. And when it is otherwise, then any modification would result from classical deformability. The relativistic limit of "rigidity" would never be approached by real material bodies.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Cracking of Lunar Mare Soil

THE tendency of lunar soil to break into clods when disturbed was recognized from Surveyor 1 photographs[1,2]. Pictures of disturbances produced in bearing tests with the Surveyor 3 soil mechanics surface sampler[3] suggested to some observers that the soil layer in Oceanus Procellarum tends to crack into thin flat "tiles" (Figs. 1*a* and 2*a*) and, therefore, that it consists of a thin, rather rigid crust over a softer substrate. Pictures of areas disturbed by the Apollo 11 closeup camera in Mare Tranquillitatis (Fig. 3*a*) and by the Apollo 12 lunar module descent engine in Oceanus Procellarum conveyed a similar impression[4,5]. None of the authors of these works were misled,

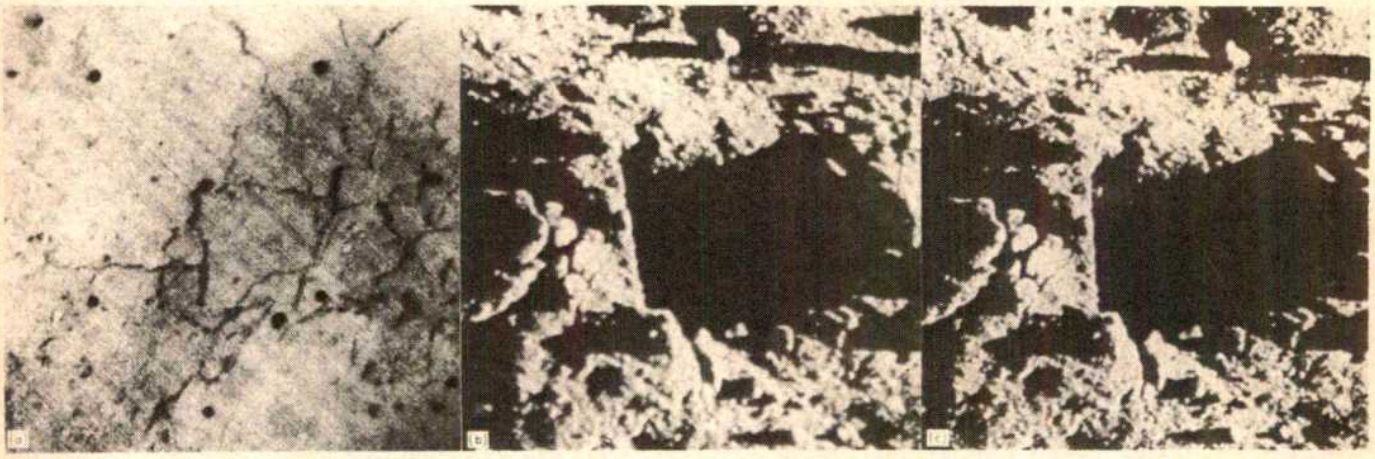

Fig. 1 Lunar surface disturbed by bearing test made with Surveyor 3 soil mechanics surface sampler (bearing test No. 2). *a*, Portion of picture made with Surveyor 3 television camera April 27, 1967, at 08 : 56 : 45 UT. View taken from west, rotated to match *b* and *c*, which are portions of photographs made with Apollo 12 hand-held camera on November 20, 1969, about 06 : 30 UT. View from south. *b* and *c* form a stereopair. (From NASA photographs AS 12–48–7106 and AS–12–48–7107.)

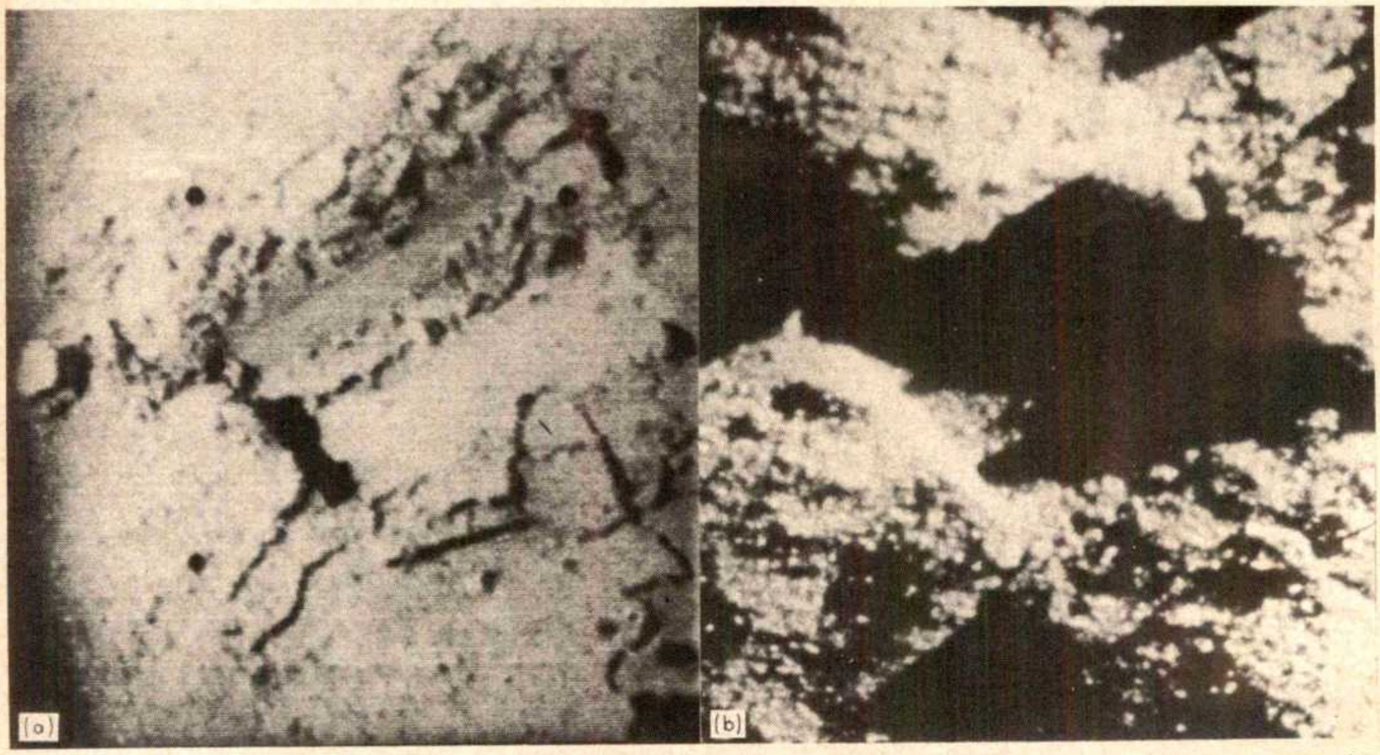

Fig. 2 Lunar surface disturbed by bearing test made with Surveyor 3 soil mechanics surface sampler (bearing test No. 5). *a*, Portion of picture made with Surveyor 3 television camera on April 30, 1967, at 15 : 39 : 30 UT. View taken from south. *b*, Portion of photograph made with Apollo 12 hand-held camera on November 20, 1969, about 06 : 35 UT. View from north, rotated to match. (From NASA photograph AS 12–48–7126.)

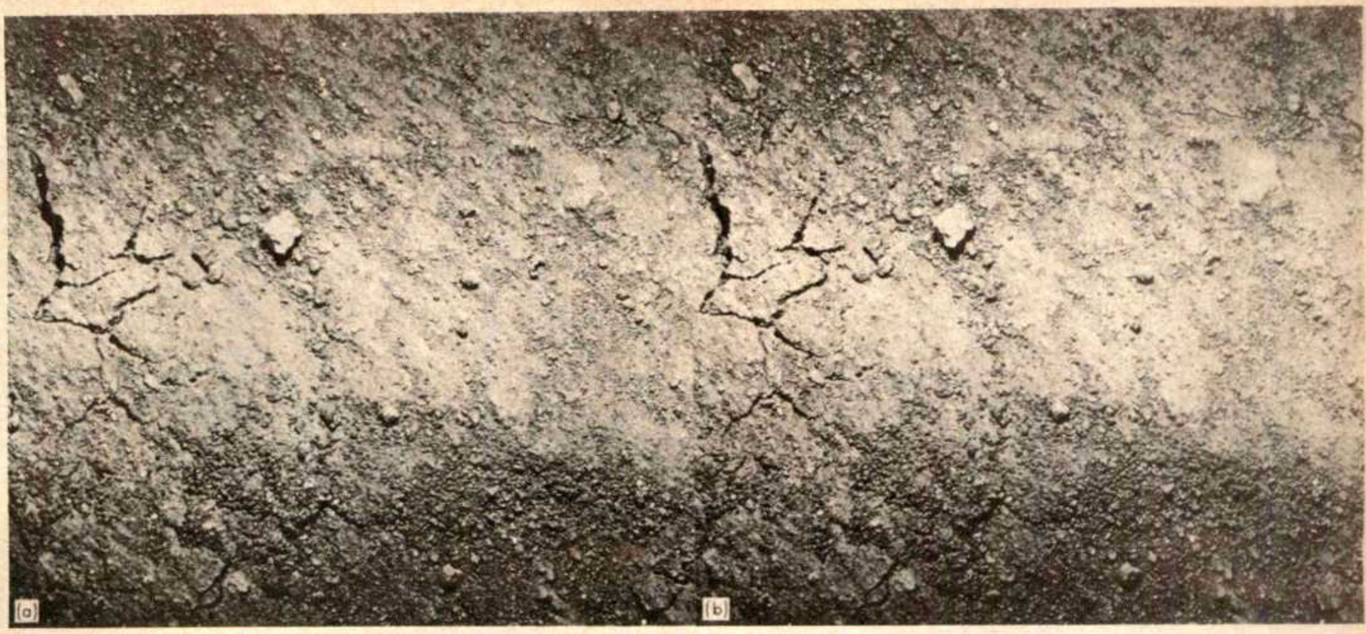

Fig. 3 Lunar surface disturbed by pressure from hood of Apollo 11 closeup camera. Illuminated by flashbulb. *a* and *b* form a stereopair. (NASA photograph AS 11–45–6702–1.)

and, indeed, they warned against this interpretation[3–5]. Nevertheless, photographs made by the Apollo 12 astronauts of the areas disturbed by Surveyor 3 help to clarify the matter.

Figs. 1*b* and 2*b* are portions of Apollo 12 photographs showing the same bearing test imprints as Figs. 1*a* and 2*a*. The appearance of the areas inboard (toward the Surveyor) is quite different: rather than a pattern of cracks in an apparently flat surface, these Apollo pictures suggest an irregular surface made up of clods or fragments. The difference in appearance arises from differences in lighting angle. The pictures in Figs. 1*a* and 2*a* were made at Sun angles of 80° and 40°, respectively, above the horizon to the west. Those in Figs. 1*b* and 2*b* were taken with the Sun 23° above the eastern horizon. The 13° slope of the crater wall on which Surveyor 3 rests makes the Sun angles to the surface about 87°, 53°, 10°, and 10°, respectively. The "flat" appearance of Figs. 1*a* and 2*a* is a result of the high Sun angle; the low angle lighting of Figs. 1*b* and 2*b* shows the topography better. The high angle lighting is useful, however, in showing the existence and extent of the pattern along which the soil broke into the clods evident at low Sun[3].

Fig. 1*c* was taken a few seconds after Fig. 1*b*, from a slightly different angle. The two figures form a stereopair. Viewed stereoscopically, they show clearly the three-dimensional character of the disturbed material; instead of flat "tiles", one sees a pile of roughly equiaxed clods.

The Apollo closeup pictures, such as Fig. 3*a*, were taken with artificial illumination at high angle above the horizontal[4]; no comparable pictures of the same areas were made with low lighting. Fig. 3*b* forms a stereopair with Fig. 3*a*; stereoviewing of the pair reveals strong vertical displacements across the "cracks". At normal stereoviewing separation angles the vertical displacements seem greater than the horizontal size of the blocks. This exaggeration effect arises from the high stereo-separation angle of the camera used[4]; the blocks are probably nearly equiaxed. The impression of flat "tiles" and "crusting", obtained by monoscopic viewing, is an illusion. Rather, the lunar soil deforms and cracks in the same manner as homogeneous isotropic terrestrial soils of moderate bulk density, having a small amount of cohesion (see refs. 1–4).

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Late Quaternary Lake Levels in the Rift Valley of Southern Ethiopia and Elsewhere in Tropical Africa

DURING the past 10 yr information has accumulated pointing to a late Pleistocene/early Holocene lacustrine period in East Africa and the Sudan Zone. On a visit to Ethiopia in January and February 1970 we made a reconnaissance study of the evidence for high lake levels of about this age in the rift valley south of Addis Ababa.

The clearest evidence of the lakes having stood higher than now is in the region of four lakes between 100 and 200 km from Addis Ababa. Lakes Ziway at about 1,652 m and Langano at about 1,590 m drain into Abiyata, 1,582 m, which in recent decades has overflowed from time to time into Shala, 1,567 m. Traces of old strand lines can easily be distinguished from the air near all the lakes and notably over an area of about 150 km^2 north of Lake Abiyata (Fig. 1).

At the beginning of this century travellers in the area reported finding sub-fossil Mollusca high above the present lake levels[1]. Nilsson recognized[2] several well developed, horizontal beaches at different levels, the most important being a terrace situated 40 m above Ziway which he placed at 119 m above Shala. (Reliable altitudinal control is not available at present and use is made of aneroid barometer readings which may be in error by some metres.) At the 119 m level, Nilsson concluded, the four Galla lakes were joined together to form a single large lake that overflowed north into the Awash valley (Fig. 2), Mohr agreed[3] with this conclusion and

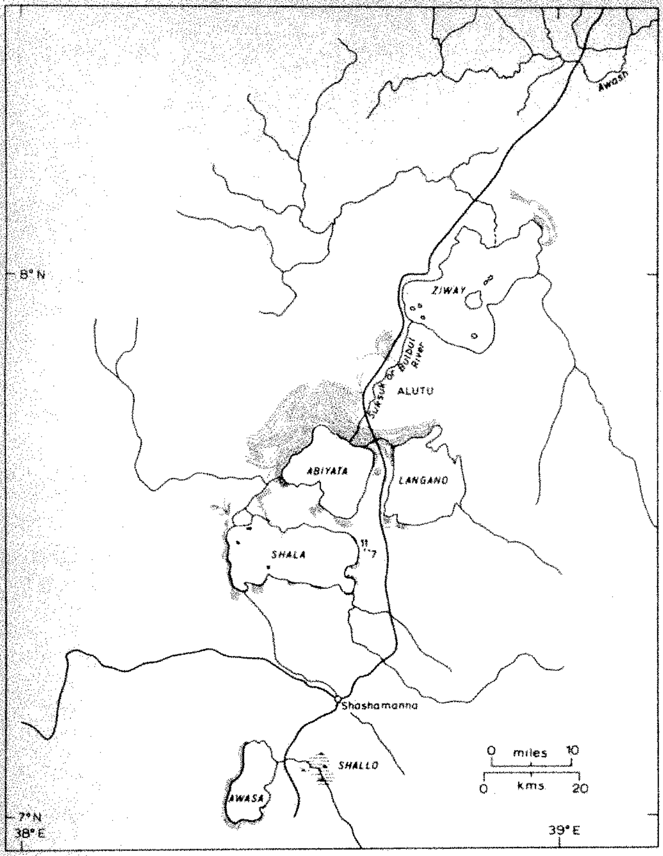

Fig. 1 The Galla lakes.

mentioned lake terraces at several levels. He noted that not all of them are developed around every lake, nor are the lowest and latest terraces always interconnected between the present-day lake basins.

The area, lying as it does within the rift, is unstable but there is no clear evidence that the old strand lines have been dislocated to any extent by faulting or tilting. The strand lines seem to mark the levels reached by lakes which formed after transverse movements that separated the rift into several more or less independent, structurally defined basins and disrupted older Quaternary lake deposits[4]. Within and around the basin occupied by the four lakes are several large, dormant volcanoes, some of which have been active in the past few centuries. It seems likely that old strandlines are particularly well developed north of Lake Abiyata because some 30 m or more of pyroclastic grits and gravels accumulated there in the old lake, after being carried by wave action and currents from the Alutu volcano from which they had either been ejected or had been eroded by gullies in the volcano's slopes. These lake sediments are exposed in the trench cut through them by the Bulbul river flowing from lakes Ziway to Abiyata.

The highest beach material possibly belonging to this lacustrine period consists of rounded cobbles which rest on a rock surface about 3 km west of Lake Ziway and at a height of 130 m above Shala which, as the lowest lake, is used henceforth as datum level. No clear beach formations, however, were found above 116 m. A beach with small fragments of gastropods occurs to the south of Lake Langano at 111 m, and lake limestones, probably formed in association with algae, were found on rocky slopes north-east of Lake Shala at 90–97 m. Several sections of lake sediments, including beds of Mollusca and shelly limestone, were exposed by gullies leading down to Shala, Langano and the Bulbul river, at various heights between 104 and 44 m above Lake Shala.

The Mollusca have been examined by Mr B. W. Sparks (Cambridge University Department of Geography), who has identified several thousand individuals belonging to sixteen species. The assemblages are comparable with those living today in large freshwater lakes in other parts of the African rift valley system. They include large numbers of *Melanoides tuberculata*, *Valvata nilotica*, *Anisus natalensis* and *Pisidium moitessierianum*. Dr P. H. Greenwood (British Museum (Natural History)) has identified a large number of very well preserved small fish bones as being principally *Barbus*, very similar to the *Barbus paludinosus* known today in some, if not all four, of these Galla lakes. A single obsidian microlith was found in beach material 89 m above Shala and 2 km east of that lake.

Samples of about 50 g of *Melanoides tuberculata* from two of the strand line deposits have been radiocarbon dated by Professor Kigoshi (Gakushuin University, Tokyo). The age calculations are based on a half-life of ^{14}C of 5,570 yr. The results are as follows: GaK 3386, 84 m above Shala (*c.* 1,651 m A.S.L.) 9,220 ± 190 BP; GaK 3387, 58 m above Shala (*c.* 1,625 m A.S.L.) 5,610 ± 100 BP.

These results suggest that about 9,240 yr ago the three southern lakes were united and were linked to Ziway which probably stood at about the same level as it does now. About 5,630 yr ago the three lakes were still (or again) united, but at a level 26 m lower.

These dates for high lake levels in southern Ethiopia are similar to those that have been obtained from other parts of the rift valley system and from the southern Sahara and Sudan Zone[5].

The Songwe river gorge has exposed fluvio-lacustrine beds formed at the margin of Lake Rukwa when it stood at a high level; clam shells in them have been dated to 8,060 ± 120 and oyster shells to 9,740 ± 130 BP[6]. Studies of saline beds, diatoms

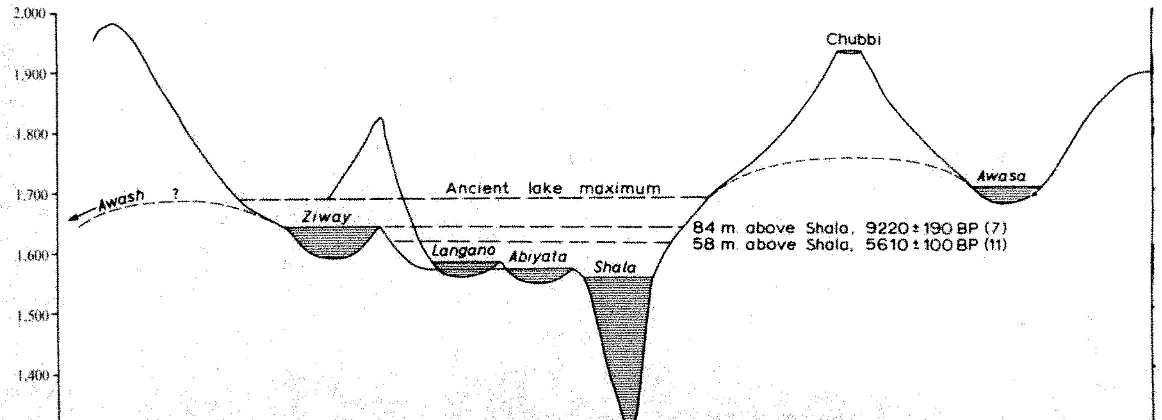

Fig. 2 NE–SW section through the Galla lakes basin.

and fossil pollen grains have shown that for some thousands of years before 12,000 BP, Lake Victoria lacked an outlet and was surrounded by savanna; then the water rose and the vegetation changed to tropical forest[7]. In the Kenya rift, a lake at a height of more than 120 m occupied the Nakuru–Elmenteita basin, about 9,650 ± 250 BP, where the lakes today are little more than large but shallow pools[8]. Between about 12,300 and 8,500 yr ago it seems that lake levels were high and then, after a phase when they dried up, the levels again rose, this time to a level of about 50 m, about 5,000 yr ago. In the Naivasha basin, immediately to the south, a deep lake existed from 9,200 to 5,650 BP and eventually dried out a little over 3,000 yr ago[9].

To the north, near the Ethiopian frontier, Lake Rudolf started to rise about 13,000 BP and seems to have stood at more than 60 m above its present level until about 5,000 BP[10]. In the Omo Valley, north of the lake, flood plain and lakeshore sediments from Member IVa of the Kibish formation have been dated to between 9,700 and 7,700 BP and from member IVb to 5,900 to 5,300 BP. These last sediments standing 80–85 m above the modern lake were laid down when Rudolf still overflowed to the Nile[11]. At the north-east corner of the lake, at Ileret, a date of 9,360 ± 135 BP has been obtained from the lacustrine (Galana Boi) beds[12]. At Lake Stefanie (Chew Bahir), less than 100 km to the north-east of Rudolf, there are lake limestones, almost certainly algal limestones of several different kinds, which contain abundant *Etheria* and some gastropods. They encrust the rocky islands at the south-east corner of the dry lake floor to a height of 20 m above the lake bed[13]. At the other end of the Ethiopian rift, in the Danakil depression of Eritrea, lake sediments have been dated to between 8,940 and 5,600 BP[13].

Whiteman has recently reviewed[15] the Pleistocene and recent history of the Sudan Republic and Wendorf *et al.* have discussed[16] the late Palaeolithic in Egypt. The sequence of deposition and erosion in the Nile Valley is difficult to interpret climatically. Very long narrow lakes stretched far up the White Nile from Khartoum leaving one terrace at 386 m that can be traced as far south as Melut and another at 382 m as far as Kosti. Shells from the latter have given dates 11,300 ± 400 (in a millenium with exceptionally high floods in upper Egypt) and 8,370 ± 350 BP.

Some of the first clear evidence of a late Pleistocene/early Holocene lacustrine period in tropical Africa came from the plains of Ténéré where Faure, Manguin and Nydal[17] obtained dates chiefly from 9,500 to 7,000 BP for lake deposits in what is now truly arid desert. At about this time Lake Chad was enormously expanded; it occupied an area of some 350,000 km^2 and overflowed by way of the Mayo Kebbi and the Benue river to the Atlantic. Mega-Chad, as the great lake has been called, may have shrunk about 7,000 BP but it was again a very large lake indeed about 5,400 yr ago[18].

The mountain massifs of Tibesti, Hoggar and Air in the Sahara together with the lake depressions at their margins provide sequences of Quaternary erosion and deposition that have been interpreted climatically. Rivers draining into Mega-Chad from Tibesti built great deltas into the lake between 10,000 and 6,000 BP according to three dates from shells collected from the base and the upper part of the formation[19]. A "middle terrace" in the mountains consists of deposits that accumulated between 12,000 and 8,000 BP and from Begour crater, in a very dry area in north-west Tibesti[20], a date of 8,295 ± 130 has been obtained from near the top of lake deposited pyroclastics about 3 m thick.

In general there are few high-level lake deposits in tropical Africa with dates between 18,000 and 13,000 BP. Between 13,000 and 7,000 yr ago it is clear that lakes were for long periods if not for the whole time higher and larger than now, when temperatures were probably similar to those of today. Lake levels seem to have been lower for the next thousand years after which they fluctuated through a smaller range. Further work on lake basins such as those in the Ethiopian rift should throw more light on the details of the sequences of climatic changes involved and the degree to which they were contemporaneous over large regions of the continent.

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Occultation of Beta Scorpii C by Io on May 14, 1971

PHOTOELECTRIC observations of the occultation of the fifth magnitude star β Scorpii C by the satellite Io (Jupiter I) on May 14, 1971, were made in Florida, Jamaica and the Virgin Islands. Some visual observations were also made. This was the first occasion on which accurate observations of such a rare event have been obtained, although several visual observations of the occultation of a star by Ganymede (Jupiter III) were made in 1911. The predictions[1] were only issued a few weeks before the event, and the track of the occultation was then very uncertain owing primarily to the uncertainty in the declination of Jupiter. It has been estimated that Io will occult a star as bright as β Scorpii C only once per millenium on average.

Photoelectric light curves and accurate timings of various portions of the event were obtained as follows: B. A. Smith and S. A. Smith monitored both immersion and emersion in ultraviolet light with a portable 20 cm telescope near Kingston, Jamaica; P. Bartholdi and F. Owen recorded immersion and emersion in blue light with a 40 cm telescope at a hilltop site in St Thomas, Virgin Islands; F. W. Fallon and E. J. Devinney measured immersion in yellow light with their 68 cm telescope near Tampa, Florida; and J. Oliver measured immersion in both blue and orange light with a 75 cm telescope near Gainesville, Florida. Another attempt by B. O'Leary, R. Brinkmann, and C. Slaughter at Guanica, Puerto Rico, was foiled by wind and clouds.

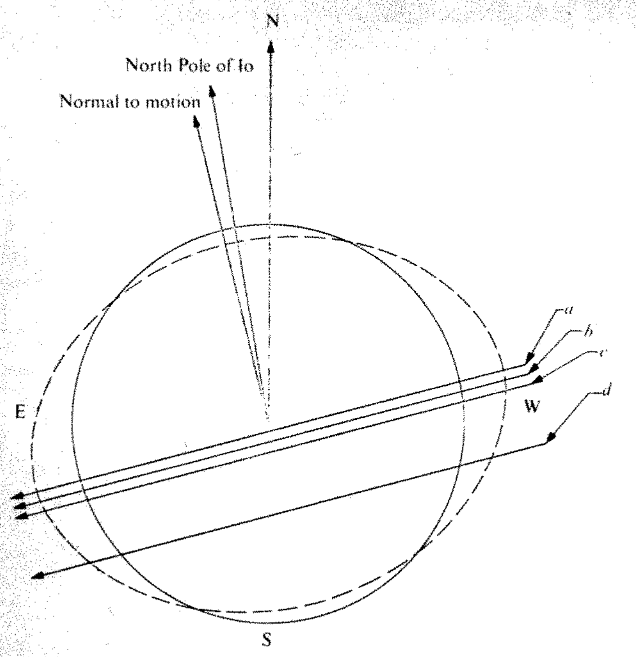

Fig. 1 Circumstances of the occultation of β Scorpii C by Io on May 14, 1971, with theoretical direction of North Pole. The tidal and rotational bulge of Io (greatly exaggerated) is shown as a dashed ellipse. *a*, Gainesville, Florida; *b*, Tampa, Florida; *c*, St Thomas, Virgin Islands; *d*, Kingston, Jamaica.

Fig. 1 shows the apparent path of the star with respect to Io, as seen from each observing site, based on the preliminary analysis of the timing data for four disappearances and two reappearances. If Io is assumed to be spherical, the deduced value of the diameter of Io is 3,659 ± 5 km. At this stage in the analysis, the data seem to be insufficient in themselves to allow a determination of the flattening, if any, of the satellite. For a homogeneous fluid body in hydrostatic equilibrium, the equatorial radius should be 20 km greater than the polar radius as seen from Earth at the time of the event, the major cause being permanent tides raised by Jupiter. It is hoped that further refinements in the reductions will yield an observed value for the flattening of Io. If de Sitter's value[2] for the mass ratio Jupiter/Io is adopted, the density of Io is found to be 2.82 ± 0.23 g cm^{-3}. The escape velocity is found to be 2.30 km s^{-1}.

None of the light curves showed any signs of an atmosphere on Io: in all cases the curves were flat just before and after occultation with abrupt changes in intensity at immersion and emersion. The presence of even a tenuous atmosphere would be indicated by a gradual change in intensity during a period of several seconds before and after occultation, caused by the defocusing of differentially refracted starlight through the gaseous medium. The observations showed that the light intensity changed by no more than a few per cent during these phases, leading to an upper limit of $\sim 10^{-4}$ mbar surface pressure for N_2 and CH_4 and $\sim 10^{-3}$ mbar for H_2. Because molecular hydrogen would most likely have escaped from a primordial atmosphere, 10^{-4} mbar is the probable upper limit for any atmosphere on Io.

Additional "events" were noted in some of the light curves. The three best defined such events are all consistent with the hypothesis that the occulted C-component of this known quadruple star system is itself a double star, with the new companion approximately two magnitudes fainter in the blue at position angle $308^\circ.2 \pm 1^\circ.2$, separation $0''.097 \pm 0''.002$.

The high resolution light curves indicated that both the decline and return to normal light were slower than that predicted by diffraction theory. This is interpreted to indicate a finite stellar diameter for the brighter C-component, which is estimated to be $0''.0002$, in good agreement with theoretical expectations.

Further details will be published by the individual authors in the near future.

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Further Evidence for a Black Hole in β Lyrae

DEVINNEY[1] has shown that the observational peculiarities of the binary system β Lyrae can best be understood in terms of the secondary mass being a collapsed star (black hole) surrounded by an opaque or nearly opaque disk. This communication points out that the recently released[2] ultraviolet photometry from the Orbiting Astronomical Observatory (OAO) leads to the same conclusion. Fig. 1 shows the light curves of β Lyrae given in ref. 2, for which the stated accuracy is ±0.01 magnitude. One might have some reservations about these observations because the shorter wavelength light curves fail to close after one cycle and the presentation (hand-drawn curves instead of the original observation points) is counter to normal practice. It may, however, be a very long time before confirming observations of this extremely interesting binary can be gathered, and they do relate in an important way to the question of whether β Lyrae contains a collapsed star. Kondo *et al.*[2] mentioned briefly the possible presence of a black hole in the system, but not for the reason advanced here.

At first glance, the eclipse of the secondary component in visible light appears reasonably deep, but most of the depression at phase 0.5 in the light curve is due to the ellipticity effect, while the actual eclipse accounts for a few hundredths of a magnitude only. The unexpected result shown by the OAO observations is that this eclipse becomes, progressively, very much deeper into the ultraviolet. Indeed, at 1380 Å, the shortest effective wavelength observed, secondary eclipse is nearly as deep as primary, and the trend strongly suggests that it becomes the deeper eclipse at shorter wavelengths.

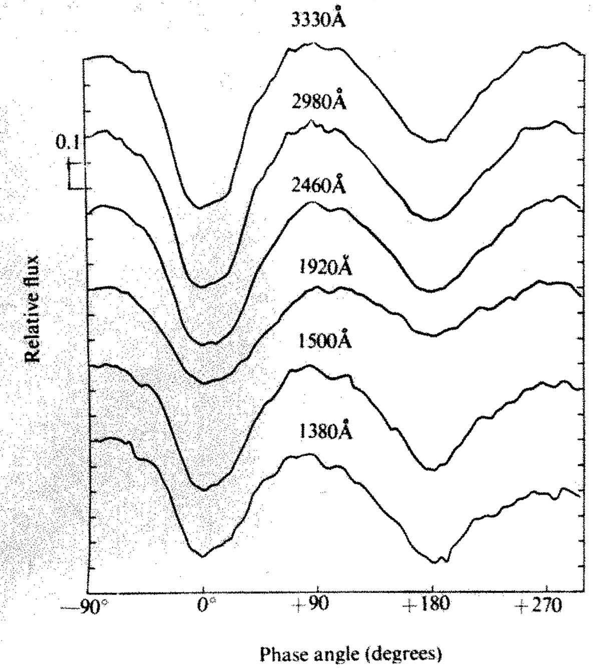

Fig. 1 OAO light curves of β Lyrae given by Kondo, McCluskey, and Houck.

Now one of the most fundamental and elementary principles in the interpretation of eclipsing binary light curves is that the ratio of the depths of the two eclipses is essentially determined by the surface brightness ratio of the two components—here the primary star and the secondary disk (since all recent models of β Lyrae involve a disk or cloud around the secondary star). For a normal binary, the component with greater surface brightness is the one of greater temperature and, because two Planckians for different temperatures are non-intersecting, this component will have the deeper eclipse at all wavelengths. For β Lyrae, however, the depth ratio changes strongly with wavelength in the opposite sense to that expected for Planckian sources, such that the roles of the primary and secondary eclipses are probably reversed shortward of, say, 1200 Å. The necessary conclusion is that the secondary continuum radiation is very strongly non-Planckian, at least insofar as its absolute intensity is concerned. That is, the light of the secondary component is unquestionably very "blue" as shown by the run of the primary and secondary depths with wavelength, and this is indicative of high temperature radiation. But it does not have the intensity (that is, surface brightness) of high temperature radiation because the secondary eclipse is a great deal shallower than primary eclipse at visible wavelengths. The secondary shines therefore by dilute high temperature radiation.

This could describe thermal bremsstrahlung from a very hot, optically thin gas, but we cannot picture this as being generated directly from the entire secondary object since the fact that the secondary causes eclipses means that it cannot be optically thin. Furthermore, its temperature would have to be very high (say 10^6 K or greater) and there is no reasonable mechanism for maintaining such a temperature. Of course, we cannot be dealing with a hot star surrounded by a cloud of intermediate optical thickness because a star as massive as is required by the spectroscopic mass function would heat the cloud to quite a high temperature and thus render it readily visible. In fact the cloud could not even exist in the radiation field of such a star for any appreciable time—the chief argument by Kondo *et al.*[2] in mentioning the black hole possibility. Thus, we are forced to a centrally localized source of high temperature continuum radiation and very modest luminosity. So far as the present evidence shows, the source itself may be either optically thin or optically thick, but in either case only a small percentage of its light can reach us directly and the exterior of the disk must shine by this light after it has undergone (typically) several scatterings.

These features of the secondary energy source—very "blue" spectral energy distribution, spatial concentration in the centre of a cloud or disk of material, and much lower luminosity than we expect for a star of the indicated mass—strongly suggest that accretion of matter by a highly condensed mass is responsible (see, for example, refs. 3, 4). Because the mass we require is of the order of 20 $M_{\odot}$, there remains only one candidate—a star which has collapsed to its gravitational radius.

I thank Dr George E. McCluskey for the light curves of β Lyrae.

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Release of Carbon Dioxide from Frozen Soil to the Arctic Atmosphere

DELINEATION of sources and sinks of CO_2 is fundamental to understanding carbon cycling in an Arctic ecosystem. Kelley *et al.*[1] observed a large, variable increase in CO_2 concentration at the tundra surface over ambient air CO_2 beginning a few days after the first snowfall. This increase continued into December, at which time CO_2 declined to relatively stable concentrations approaching ambient air levels. CO_2 at the surface increased from early May to late June until the snow disappeared. Bashenina[2] also observed CO_2 concentrations under the snow higher than atmospheric values. The present investigation was undertaken to explain the source of the subnivean CO_2.

Soil cores, 2.5 cm in diameter, were collected from five sites in northern Alaska during September 17–20, 1970. The cores included organic and mineral material extending from the tundra surface to the level of permanently frozen ground. Core length averaged 24 cm ranging from 17 to 31 cm. The cores were sealed, weighed, and stored at 4°–10° C until subjected to laboratory analysis.

The cores were weighed at the time of analysis to verify that water loss during storage was less than 1%. They were then cooled to freezing temperatures during which CO_2 was monitored by infrared gas analysis. This was accomplished by placing the cores in a 2.5 cm diameter cylindrical 'Pyrex' chamber with ball and socket joints to accommodate air intake and outlet, and a thermocouple to monitor core temperature during analysis. An ascarite cell in the intake line provided CO_2 free air to the core. CO_2 detected by the analyser in the outflowing air stream was concluded to be of core origin.

A series of accurately controlled CO_2 reference gases was used to calibrate the analyser. CO_2 from the cores and temperature were recorded simultaneously on a two-channel strip chart recorder. Total water content and *p*H were determined for each core subsequent to freezing.

The section of the CO_2 curve of particular interest in this investigation (Fig. 1) corresponds to the period of phase change of the soil moisture. An important assumption was made that the evolved CO_2, represented by the area under the curve in Fig. 1, above the dashed line, must be due to freezing of the core. A biological source is ruled out or diminished in importance in that biochemical reaction rates normally vary directly with temperature. Since core temperatures were held

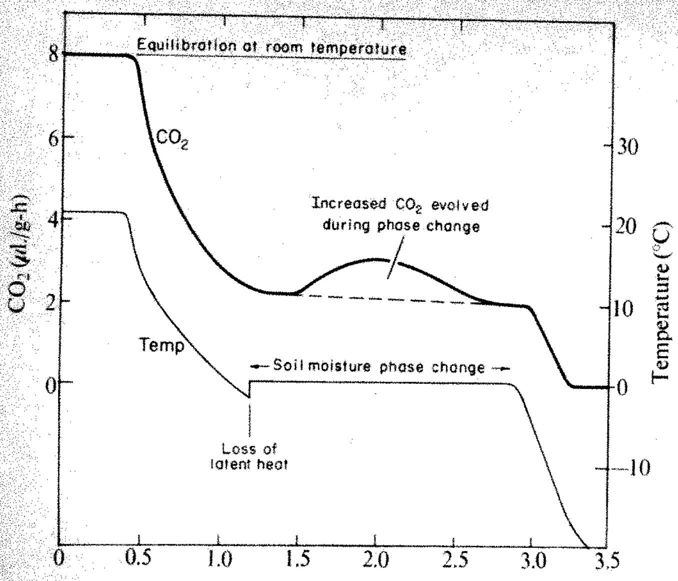

Fig. 1 Evolution of CO_2 relative to temperature from a freezing tundra soil core.

constant at 0° C during phase change, CO_2 production from biological sources would be expected to remain constant or perhaps be inhibited by solidification of the soil water.

The results of the analyses are shown in Table 1. Assuming the lowest CO_2 quantity (0.1 μl./g) observed reflects the natural system and is constant over the tundra surface, approximately 500 l./Ha would be released from the surface 30 cm by the freezing process. A corresponding release for the highest observed value (2.0 μl./g) would be 90,000 l./Ha. The CO_2 thus released from solution apparently escapes to the atmosphere at varying rates throughout the period when soils are frozen. Greatest rates of escape occur in the autumn and spring[1].

During the summer, decomposition within the active layer of tundra results in a soil saturated with CO_2 (ref. 3). As the soil freezes, CO_2 should be evolved. Unlike the trapped gas that appears in the centre of an ice cube when a volume of water is frozen, a soil core represents a different situation. The presence of plant roots, organic matter, and soil particles allows many routes for entrained gas to escape.

Table 1 Carbon Dioxide Concentrations evolved from Freezing Tundra Soil Cores

Habitat	CO_2 μl./g dry soil	*p*H	Moisture content % wt
Umiat—Colville River floodplain	1.5	4.4	97.4
	1.0	4.9	77.9
	0.8	4.5	89.1
	0.5	4.7	92.9
	0.9	4.6	116.0
	1.2	4.9	83.3
	0.7	4.7	62.7
	0.9	4.9	66.5
	2.0	5.1	67.4
Barrow—wet sedge meadow	0.4	3.7	57.5
	0.3	3.7	76.4
	0.1	3.8	46.8
	0.1	3.7	54.9
	0.7	3.9	109.1
	0.6	4.1	63.8
Barrow—marsh	0.1	4.5	44.3
	0.2	5.1	40.9
	0.2	5.1	46.1
	0.1	5.1	44.8
	0.1	4.8	53.3
Barrow—raised beach ridge	0.1	4.3	30.1
	0.1	4.3	36.6
	0.7*	5.2	51.6
Barrow—raised beach ridge	0.1	5.2	33.8
	0.8	5.2	34.5
	0.2	5.0	38.9

* Data for this core are graphed in Fig. 1.

The "ice cube" effect was apparently observed when autoclaved bentonite saturated with CO_2 enriched water was rolled into cores and subjected to the same freezing treatment as the soil cores. No increase in evolution of CO_2 occurred on freezing. The possibility that a high proportion of the CO_2 remained dissolved in unfrozen, interfacial water in the clay core cannot be discounted, however[4].

Cores that provided the highest evolution of CO_2 were characterized by coarse texture and high moisture content. Cores collected from a sandy bluff along the Meade River 100 km south of Barrow were relatively dry and showed no increase in CO_2 evolution on freezing (not included in Table 1). Cores from a beach ridge near Barrow which contained much gravel mixed with silt and clay size particles and with 5 to 15% higher moisture content than the Meade River cores had detectable CO_2 evolution.

The cores in this investigation were frozen from the surface to the centre. The tundra, however, freezes bidirectionally. Sub-freezing temperatures at the soil surface and at the upper surface of the permanently frozen ground give rise to two freezing fronts. As these two fronts approach each other in the autumn, CO_2 is evolved into the unfrozen layer. Some of the CO_2 may escape to the tundra surface in proportion to texture, cracking, and other avenues of escape producing a highly variable autumn rise in CO_2 concentration as observed by Kelley *et al.*[1]. Some CO_2 may become trapped within the freezing active layer and may slowly escape causing a soil surface CO_2 level slightly higher than ambient air during the winter months.

Associated with the increase in tundra surface temperatures in the spring is an increase in the subnivean and ambient concentrations of CO_2. Further release of trapped gas as a result of differential warming of the soil may be the source of the spring rise reported by Kelley *et al.*[1]. Amplification of this spring rise by biological systems cannot be ruled out once minimal conditions for growth and assimilation are met.

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BIOLOGICAL SCIENCES

Actin in Sperm Tails and Meiotic Spindles

IN many cases cellular motility seems to be due to interactions between actin and myosin[1-8]. Actin (or actin-like material) has also been identified in other cellular systems which exhibit motility[9-14] and actin-like and myosin-like proteins have been claimed to be isolated from mitochondria[15] and chloroplasts[16]. While it is not proved that motility in these systems is due to actin and myosin, actin-myosin interactions are probably involved. Flagellar (ciliary) motions and chromosome movements, on the other hand, have generally been attributed to microtubules[17–19], and thus there seemed to be two different kinds of motile systems; one based on actin-myosin interactions and the other on microtubules. We have found, however, actin-like filaments in both sperm tails (flagellae) and meiotic spindles of crane flies. Although we are well aware that we have demonstrated merely the presence of actin and have by no means proven that the flagellar and spindle actin has anything to do with motility, we nonetheless suggest that motility in all motile systems in higher cells is based on actin-myosin interactions.

We glycerinated crane fly testes (*Nephrotoma suturalis* Loew) in a 1 to 1 mixture of pure glycerol and standard salt solution[11]. All the cells in any one testis are in roughly the same stage of maturation, and in different experiments we used testes with cells in division, or with spermatids, or with mature sperm. After 3 days glycerination, the cells were removed from the testes and processed for electron microscopy, either for negative staining with 1% uranyl acetate[20] or for embedding and sectioning. For negative staining, the cells were first ruptured in standard salts solution; some aliquots were incubated with heavy meromyosin (HMM)[21] before negative staining, other aliquots were incubated with HMM and ATP, whilst other aliquots were negatively stained directly. For embedding and sectioning, glycerinated cells were incubated for 24 h with HMM, and then fixed with 2% glutaraldehyde, postfixed with 1% osmium tetroxide, and processed using standard techniques[20].

Actin was prominent in negatively stained preparations of spermatids and mature sperm. The actin was identified as such by its characteristic appearance and dimensions[21], and by the facts that it bound HMM to form characteristic arrowheads[21] and that ATP inhibited arrowhead formation[21]. The individual actin filaments were about 50 Å in diameter but very often were packed into bundles which were up to around 800 Å wide and which were several microns long (Fig. 1*a*). There were as many as fifteen to twenty filaments per bundle. In any one bundle the actin filaments were often of opposite polarities, that is the HMM arrowheads on adjacent actin filaments often pointed in opposite directions (Fig. 1*b*). These actin-containing bundles of filaments are distinguishable from axoneme microtubules morphologically and by the absence of HMM binding to microtubules.

We examined by electron microscopy sections of one cell in anaphase and several metaphase cells, the stages having been determined by light microscopy. We saw some HMM-reacting filaments in the spindle areas. These actin-like filaments had the characteristic appearance of "fluffy" filaments after HMM-binding[10,11]. Some of the actin was near chromosomes, oriented in the pole-to-pole direction, and in some sections a few filaments might have been attached to the poleward side of some chromosomes. There was also actin near the spindle poles and at the cell periphery.

Although we cannot prove that actin from sperm or spindle is involved in sperm or chromosome motion, it would be surprising if this were not so. The presence of actin in other motile systems, together with the identification of actin in sperm tails and spindles, strongly suggests that actin-myosin interactions are responsible for all kinds of motility in higher cells.

Our identification of actin in sperm tails confirms earlier biochemical indications that sperm tails contain actin-like and myosin-like components which react with muscle myosin and actin, respectively[22,23], and that a myosin-like component in cilia reacts with muscle actin[24,25]. The identification of actin in spindles confirms earlier evidence from isolated sea urchin mitotic apparatus. Aronson[26] found that fluorescent-labelled HMM binds to isolated mitotic apparatuses, and Miki-Noumara[27] found a 2.3S component of isolated mitotic apparatus that was like actin in that its viscosity increased when it was transferred from KI solution to one with ATP.

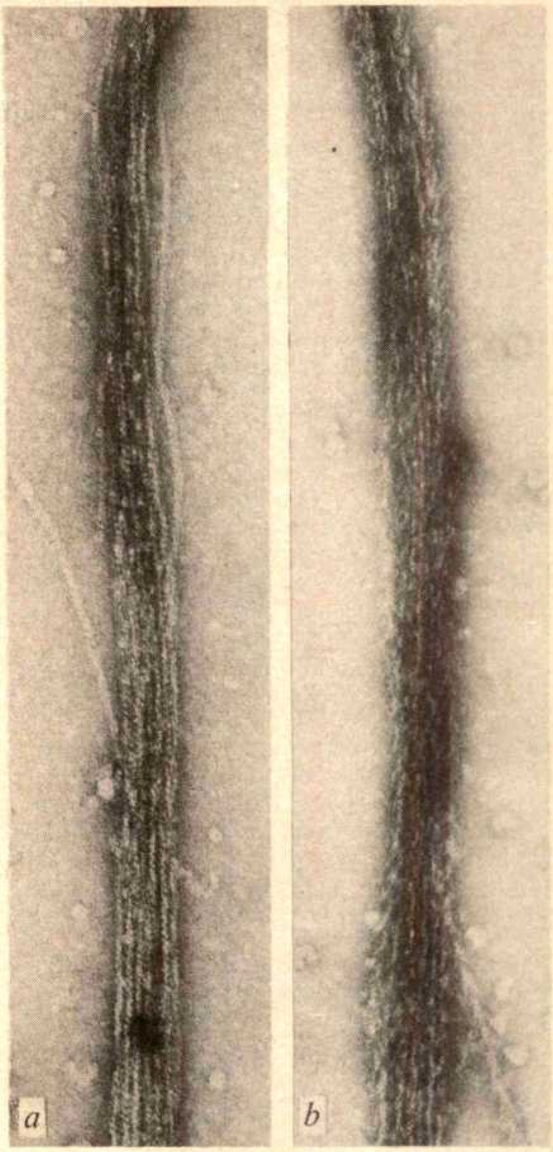

Fig. 1 *a*, Negatively stained preparation of bundle of actin filaments from mature *Nephrotoma* sperm (×131,000). *b*, Bundle of actin filaments from mature *Nephrotoma* sperm reacted with HMM. The opposite polarity of two of the filaments can be seen (×113,000).

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Actin in the Mitotic Spindle

I PREVIOUSLY suggested that the shape of the metaphase spindle cannot be maintained if there is tension in the component microtubules[1]. Spindle tension has been detected[2,3] and could be due to some other component pulling the chromosomes over the rigid microtubular framework.

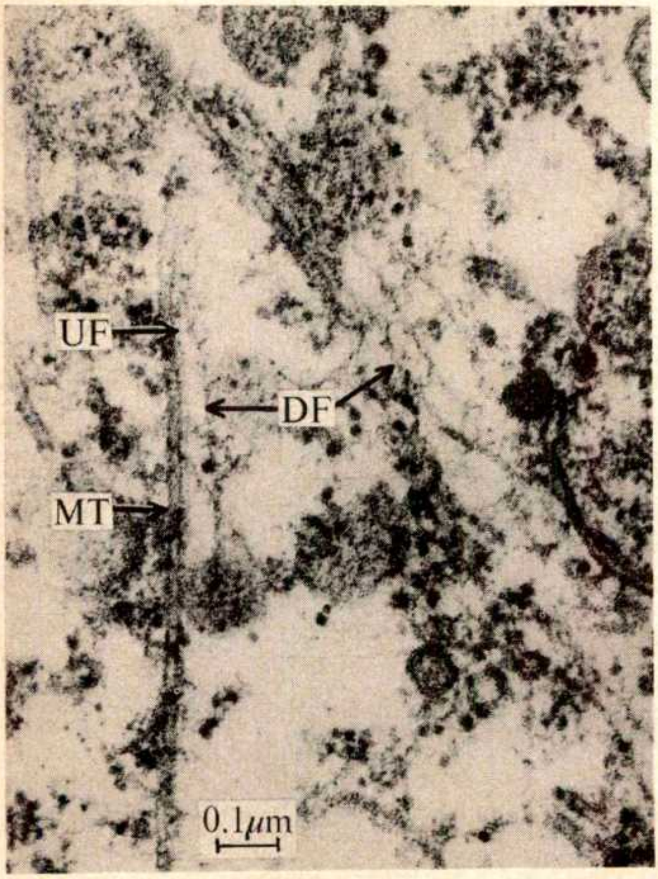

Fig. 1 Part of a metaphase mitotic spindle, long axis of spindle running from top left to bottom right of picture. Oriented, decorated filaments (DF) are shown, and an undecorated filament (UF) associated with a microtubule (MT) (×108,500).

Aronson[4] established that fluorescein-labelled heavy meromyosin (HMM) binds to isolated sea-urchin spindles as well as to muscle fibrils, indicating that actin is present in both. I have now located the actin in electron micrographs with the method used by Ishikawa *et al.*[5].

Locust testis tissue was treated for 24 h at room temperature with 50% glycerol in a buffer containing 0.1 M KCl, 0.006 M phosphate, and 0.005 M $MgCl_2$. The testis follicle wall was torn slightly with a glass needle and the tissue was incubated for a further 24 h with rabbit HMM in a similar buffer at 4° C. The tissue was fixed in 2.5% glutaraldehyde treated with 1% osmium tetroxide, and embedded in araldite. Sections were stained with uranyl acetate and lead citrate.

Mitotic cells of the testis were studied because their spindle microtubules survive glycerination and incubation, whereas spindle microtubules in meiotic cells do not. Three types of filament, in addition to microtubules, can be seen in metaphase mitotic cells. One type runs parallel at a distance of 100 Å to an associated microtubule but there are no apparent cross links (Fig. 1). This type of filament is never associated with heavy meromyosin. Another type forms a complex with HMM, which characterizes the filament as actin. Most of these filaments lie parallel to the long axis of the spindle but are not closely associated with any microtubules. The third type of filament is found at the periphery of the cell, parallel to the surface, and always forms a complex with HMM. It is found in all testis cells, whether in division or not.

Although actin has only been shown to be present in the spindle, it is probably involved in the movement of chromosomes in which case chromosome movement would involve, like many other cell movements[6,7], an interaction between actin and myosin. The observations suggest that either the microtubules themselves have myosin-like properties or they are associated with myosin which is lost during preparation of the tissue.

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Protein Polymorphism

IN their well known study of protein polymorphism in *Drosophila pseudoobscura*, Prakash, Lewontin and Hubby[1] showed that most loci reveal little or no differentiation in allele frequencies in different sub-populations; they concluded that the observed polymorphisms cannot be due to random genetic drift of neutral mutations and are most likely to be caused by some form of balancing selection. This conclusion has been challenged by Kimura and Ohta[2] on the grounds that only a small amount of migration between the sub-populations is required to make them into an effectively single panmictic population in which one would not expect to find much local differentiation in allele frequencies under the neutral mutation theory originally proposed by Kimura[3]. The purpose of this letter is to point out another feature of the data of Prakash *et al.*[1] which suggests that the polymorphic alleles are not selectively neutral.

Table 1 shows in a simplified form the results of Prakash *et al.*[1] for loci with three or more alleles. (The esterase-5 locus is excluded because it is clearly different from the rest, no fewer than twelve alleles having been identified; the data for the isolated population around Bogota are also excluded since this population is much less variable, probably on account of genetic drift.) The alleles are given in the order of electrophoretic mobility, and have been classified arbitrarily into rare alleles (with a frequency less than 10%) and common alleles (with a frequency greater than 10%). There is a marked tendency for the rare alleles to occur at the beginning or the end of a sequence and for the common alleles to occur in the middle of a sequence; for example, when there are two rare alleles and one common allele the sequence is always RCR and never CRR or RRC. If these alleles are selectively neutral one would expect all possible orders of the sequences to be equally likely; on the other hand, this kind of result would be expected if there is an optimal genotype, which may be heterozygous or homozygous, and if the difference in electrophoretic mobility of two alleles can be regarded as a crude measure of their functional difference.

Table 1 Data of Prakash *et al.*[1] on Polymorphism in *Drosophila pseudoobscura*

Population	Strawberry canyon	Mesa Verde	Austin	Probability of observed type of sequence in most polymorphic population
Locus	Allele 1 2 3 4 5	Allele 1 2 3 4 5	Allele 1 2 3 4 5	
Pt-7	R R C R	– R C R	– R C R	$\frac{1}{2}$
Leucine aminopeptidase	R R C R –	R R C R –	R R C R R	$\frac{1}{5}$
Pt-8	R C C –	R C C R	R C C R	$\frac{1}{6}$
Xanthine dehydrogenase	R R C C R	R R C C R	R R C C R	$\frac{1}{5}$
Larval acid phosphatase	– C –	– C –	R C R	$\frac{1}{3}$
Acetylaldehyde oxidase-2	R R C R	– – C –	– – C –	$\frac{1}{2}$
Octanol dehydrogenase-1	– C R	R C R	– C –	$\frac{1}{3}$
Pt-10	R C C	R C R	R C R	$\frac{2}{3}$
α-Amylase-1	R C C	– C C	– C C	$\frac{2}{3}$

R, rare (frequency <0.1); C, common (frequency >0.1); –, not present in this population; blank, no such allele present in any population.

To test this hypothesis the probability of each type of sequence was calculated on the assumption that all arrangements are equally likely; for example, the probability of RCR is one-third because there are three arrangements of which only one has C in the middle, the probability of RCCR is one-sixth since there are six arrangements of which only one has two Cs in the middle, and the probability of RCC is two-thirds since there are three arrangements of which two have an R at the end. Because of the high correlation of the allele frequencies in the different populations, it would clearly be wrong to count all the sequences as independent observations. For each locus the sequence from the most polymorphic population was therefore used, and the probability of the type of sequence in this population is shown in the last column of Table 1. Because each observed sequence was of the most extreme type, it is possible to obtain an overall significance level by multiplying these probabilities together. This procedure gives a probability of 1/12,150.

It can be concluded that each type of sequence is not equally likely. This finding is incompatible with the theory, advanced by Kimura[3] and Kimura and Ohta[2], that protein polymorphism is due to random genetic drift among a large number of neutral isoalleles in a finite population of fairly constant size. The most plausible alternative theory is that the alleles involved are not selectively neutral.

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Ultrafiltration in the Gastropod Heart

IT is generally agreed that the urine of most molluscs is produced initially by ultrafiltration of the haemolymph into the pericardial cavity, and that the composition of this initial filtrate is modified by the kidney before being expelled as urine[1-7]. The only exceptions are the terrestrial pulmonate gastropods, in which urine seems to be filtered directly into the kidney[8,9]. Pierce[10], however, is not convinced that the heart is the filtration site in lamellibranchs, and suggestions that ultrafiltration occurs through the wall of the auricle in most gastropods were not substantiated by ultrastructural studies of terrestrial and freshwater pulmonates[11].

Using the snails *Poteria lineata* and *P. varians* (Gastropoda, Prosobranchia, Cyclophoridae) collected from forest leaf litter in Jamaica we have shown that urine is initially produced by filtration into the pericardial cavity; electron microscopy has suggested that the ventricle, not the auricle, is the main site of filtration.

Although few figures are available, the similarity between the composition of the haemolymph and that of pericardial fluid (Table 1) suggests the origin of the latter by filtration. This was demonstrated by injecting ^{14}C-inulin, dissolved in *Poteria* Ringer solution, into the rectal sinus of *P. varians*, and removing samples of about 2 μl. at intervals from the efferent pulmonary vein (leading directly into the auricle) and pericardial cavity. The concentration of inulin in the pericardial fluid rose rapidly to a value slightly higher than that in the haemolymph, and remained so for a range of 2,000–200 c.p.m./μl. (Fig. 1). Presumably this slight difference is main-

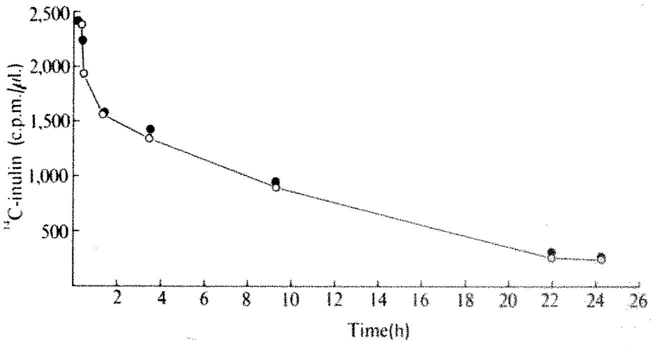

Fig. 1 The concentrations of inulin in haemolymph (open circles) and pericardial fluid (closed circles) of *P. varians* following injection of ^{14}C-inulin into the rectal sinus at time zero.

Table 1 Comparison between the Composition of Haemolymph and that of Pericardial Fluid in *Poteria lineata*

	Osmotic pressure mmol/l. NaCl	Na mmol/l.	Ca mmol/l.	Mg mmol/l.	Cl mmol/l.
Haemolymph	40.8 ± 1.13 (9)	31.4 ± 0.80 (9)	5.1 ± 1.04 (9)	1.5 ± 0.34 (9)	25.1 ± 0.85 (9)
Pericardial fluid	40.7 ± 0.35 (3)	32.0 (1)	3.9 (2)	1.4 (2)	23.0 ± 2.13 (3)

Values are given as mean ± s.e. (number of observations).

tained because it takes a certain time for the fluid to be filtered: fluid present in the pericardial cavity at any one time was filtered from the haemolymph when the latter had a slightly higher concentration of inulin. These results suggest that haemolymph is filtered through the heart into the pericardial cavity. The situation is similar to that in the aquatic prosobranch *Viviparus*.

The outer surface of the auricle is lined by a discontinuous squamous epithelium of seemingly inactive cells with dense cytoplasm and interdigitating branches, but over the ventricle this is replaced by cells (Fig. 2, po) which resemble the podocytes of the mammalian glomerulus[12], and the coelomic sac of the crayfish *Cambarus*[13], both of which are thought to be concerned with ultrafiltration. Active and senescent cells can be distinguished (Fig. 2). The wall of the ventricle is devoid of an endothelium and its network of muscle fibres is embedded in connective tissue permeated by numerous channels extending from the central lumen to the basal lamina of the epithelium. At the distal ends of the channels the lamina is the only barrier between the haemolymph and the epithelium and these are taken to be the filtration sites (f.s.).

The epithelial cells are raised above the basal lamina by stilt-like processes of the cytoplasm (pr), creating subcellular spaces (sp), which presumably receive the filtrate and open into the pericardial cavity through narrow intercellular channels. Their cytoplasmic processes give rise to fine branches (pe), similar to pedicels, which interdigitate with those of neighbouring cells.

Apart from the absence of a fenestrated endothelium the arrangement is similar to that in the glomerulus, suggesting that in *Poteria* ultrafiltration occurs in the ventricle rather than in the auricle. Since the hydrostatic pressure of the haemolymph presumably reaches its maximum in the ventricle, this would also suggest that it is the more likely site.

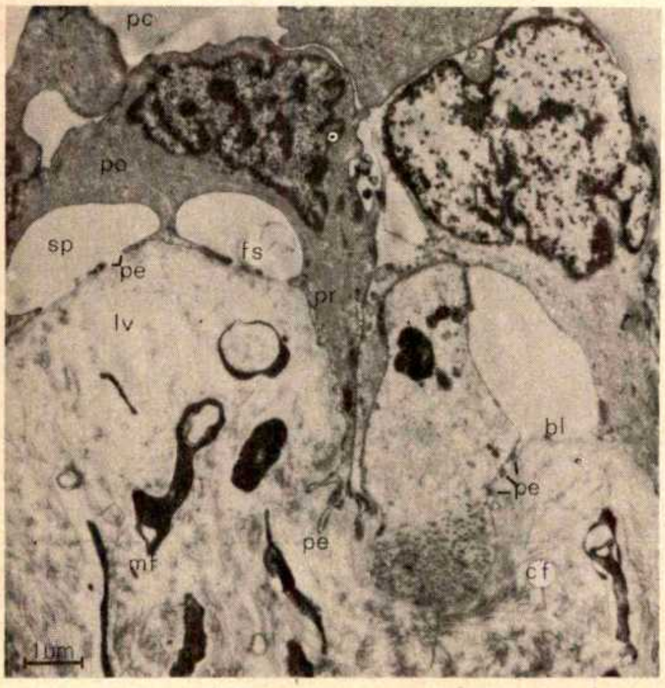

Fig. 2 Electron micrograph of the epithelium and part of the wall of the ventricle of *P. lineata*. An active podocyte is shown on the left, a senescent one on the right.

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Immunoelectron Microscopic Studies of Type C Virus Particles in ESP-1 and HEK-1-HRLV Cell Lines

A MONOLAYER cell culture (ESP-1) established with cells from pleural effusion of a patient with Burkitt lymphoma (American type) continuously produced virus particles morphologically similar to murine type C virus particles[1]. Earlier results[1] of immunodiffusion tests suggest that the type C virus particles in the ESP-1 culture do not seem to have the group specific (gs-1) antigen of the known animal leukaemia viruses. These immunodiffusion tests also did not show the gs-3 antigen common to the viruses of leukaemia of mouse, hamster, rat, and cat.

We now describe studies carried out by the indirect immunoferritin labelling technique[2,3] on the type C virus particles of the ESP-1 cell line. The extreme sensitivity of the immunoferritin technique in specific labelling of individual virus particles[4-6] provides a valuable tool for study of morphological and immunological properties of virus particles in the ESP-1 cell line. Type C virus particles in the human embryo kidney cell culture infected with the murine Rauscher leukaemia virus (HEK-1-HRLV) were used for comparison.

Antisera to MuLV gs and type-specific antigens were obtained from adult $(W/FU \times BN)F_1$ rats with growing transplants of a leukaemia induced in an inbred W/FU rat by wild type Gross virus[7]. By immunodiffusion and immunofluorescence tests, these antisera contained gs-1 but lacked gs-3 antibody[7]. Monospecific antibody to the gs-3 antigen was made by immunizing rats with the antigen-antibody precipitin band made by using antisera selected for their reaction to feline leukaemia virus antigen (the gs-3 being represented as the antigen in the anti-gs-3-gs-3 complex). The band was cut from the agar and washed with saline before immunization of the rats. The resulting antiserum contained antibodies monospecific for the gs-3 antigen. The reagents were shown to be monospecific by immunodiffusion test (carried out by G. Geering) and by immunofluorescence test (carried out by Dr J. Hilgers). (Both antisera were supplied by Drs Lloyd J. Old and Gayla Geering.)

Experiments carried out to determine the dilution of serum most satisfactory for use in ferritin labelling showed that dilutions lower than 1 : 20 produced much non-specific labelling[6].

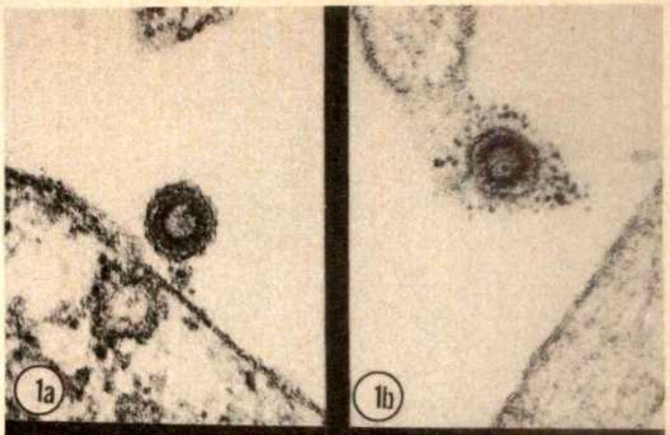
The virus particles in the ESP-1 cell culture were not labelled with ferritin by the rat anti-MuLV (gs-1) serum followed by treatment with ferritin conjugated goat anti-rat IgG (Table 1 and Fig. 1*a*). Virus particles in the HEK-1-HRLV cell line were strongly labelled by the same treatment (Fig. 1*b*). Although gs-1 antigens are considered internal viral antigens, this test clearly shows that the virus particles are labelled on the viral envelope. Similar labelling was also observed on the viral envelopes of other murine leukaemia virus treated with the same antiserum: type C virus particles in the cells of SJL/J/Cr spleen culture, in induced BALB/c/Dm strain mouse mammary tumour, in spontaneous RIII/Dm strain mouse mammary tumour (D-W) cell line producing A, B, and C particles[5-8]. Type B virus particles in a (C57 × Af)F1 spontaneous mammary tumour cell line and in the spontaneous RIII/Dm strain mouse mammary tumour culture (D-W) were not labelled with the anti-gs-1 serum[6].

The results of these tests indicate that the gs-1 antigen of the type C virus particles found in the ESP-1 human cell culture differs from the gs-1 antigen of the Rauscher murine leukaemia type C virus particles adapted to the human embryo cell line and from that of other murine type C viruses tested. These tests were repeated and resulted in identical findings[9].

Table 1 Results of Immunoferritin Tests on Type C Virus Particles in the ESP-1 and HEK-1-HRLV Cell Cultures

Sera used	ESP-1	HEK-1-HRLV
(*a*) Rat anti-MuLV (gs-1) untreated, diluted 1 : 20 and 1 : 64	–	+
(*b*) Rat anti-MuLV (gs-3) untreated, diluted 1 : 20 and 1 : 64	+	+
(*c*) As (*b*) and absorbed with guinea-pig kidney powder and sheep red blood cells, diluted 1 : 64	+	NT
(*d*) As (*b*) and absorbed with pelleted Rauscher leukaemia virus, diluted 1 : 64	–	–
(*e*) As (*b*) and absorbed with pelleted Gross leukaemia virus, diluted 1 : 64	–	–
(*f*) As (*b*) and absorbed with pelleted feline leukaemia virus, diluted 1 : 64	–	–
(*g*) Controls Rat anti-MuLV (gs-3) serum 1 : 64 followed by treatment with ferritin conjugated normal goat IgG	–	–
Normal rat serum 1 : 20 followed by treatment with ferritin conjugated goat anti-rat IgG	–	–

NT, not tested.



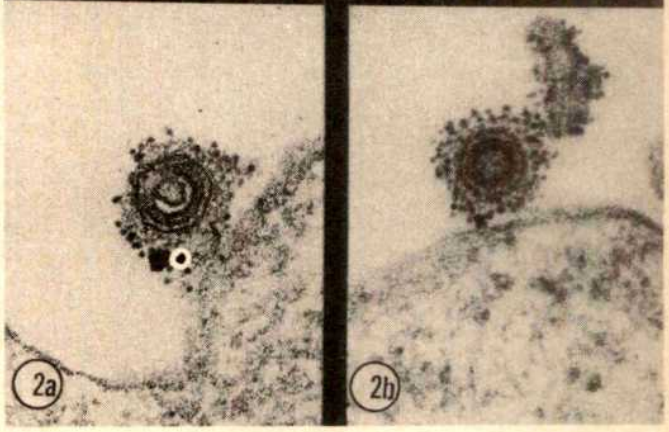


Fig. 1 *a*, Thin section of ESP-1 tissue culture treated with rat anti-MuLV (gs-1) serum followed by ferritin conjugated goat anti-rat IgG. No labelling of type C virus particle (× 90,000). *b*, Thin section of human embryo kidney tissue culture infected with Rauscher murine leukaemia virus (HEK-1-HRLV). Same treatment as *a*. Labelling of type C particle (× 90,000).

Fig. 2 *a*, ESP-1 tissue culture treated with rat anti-MuLV (gs-3) serum followed by ferritin conjugated goat anti-rat IgG. Ferritin labelling of type C particle (× 90,000). *b*, HEK-1-HRLV tissue culture, same treatment as in *a*. Ferritin labelling of type C particle (× 90,000).

Virus particles in both cell cultures were labelled by ferritin with the rat anti-MuLV (gs-3) serum (Figs. 2*a* and *b*). The labelling was not removed by absorption with Forssman antigens but removed by absorption of the serum with high-speed pellets of either Rauscher leukaemia virus obtained from spleen of infected (CFW-2) mice (obtained from Hazelton Labs), or with gross leukaemia virus obtained from spleen of NIH BALB/c mice (from Germfree Products, Inc.) (Table 1). Absorption with high-speed pellets of feline leukaemia virus (from Electronucleonics, titre 1×10^9/ml.) also removed the labelling of type C virus particles in both tissue cultures (Table 1). These results indicate that the ESP-1 virus particles share an antigenic determinant similar to the group specific, gs-3 (interspecies antigen) of the mammalian leukaemia viruses[7,10].

The presence of the gs-3 antigenic determinant in the ESP-1 virus particles as shown by these tests, compared with the earlier negative results of immunodiffusion tests[1], may be explained by the high sensitivity of the immunoferritin technique. These observations indicate an antigenic relationship between the particles in the ESP-1 human cell culture and those virus particles present in leukaemia and sarcomas of animals.

The presence of a similar group specific antigen (gs-3) in the ESP-1 cell culture is supported by the fixed immunofluorescence test (Priori, unpublished data) using the same rat anti-MuLV (gs-3) serum and rabbit anti-feline leukaemia virus serum (from Dr W. D. Hardy).

We understand that the presence of murine leukaemia virus group specific antigen has been recently observed in the ESP-1 human cell line by immunodiffusion[11]. Further studies are needed to explain the difference between those results and those of our present findings.

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Antibody and Plant Agglutinins stimulate Phagocytosis of Erythrocytes by *Acanthamoeba*

AXENICALLY grown *Acanthamoebae* phagocytose in simple media a wide variety of particulates while exercising particle discrimination[1], and for studies of particle recognition they provide a useful alternative to vertebrate phagocytes[2]. We have shown that the uptake of sheep erythrocytes (SE) by the amoebae is increased by antibody to the red cells, as with mammalian macrophages. However, the mechanism of opsonization by antibody seems to differ in this case. Furthermore, ingestion of SE by the amoeba was enhanced by plant agglutinins.

Acanthamoeba sp. were supplied by Dr R. J. Neff[3], and phagocytosis was assessed microscopically or measured by spectrophotometry of amoeba extracts after osmotic lysis of uningested red cells[1]. Rates of uptake[4] were obtained from absorbances at 30 and 60 min and are expressed in absorbance units/10^6 amoebae/min. All rates are averages of triplicate determinations. Rabbit antiserum (titre 1:3,200) was obtained after repeated intravenous injections of washed SE.

Whereas control SE were ingested at rates of 0.0001 to 0.0010 in different experiments (0.2 to 2.0 red cells ingested per amoeba in 60 min), addition of antiserum consistently stimulated red cell uptake. In a typical experiment ingestion rate in the controls was below 0.0001; with antiserum added to the amoeba-red cell mixture at dilutions of 1:400, 1:800 or 1:1600, ingestion rates were respectively 0.0174, 0.0113 and 0.0035 units. These results were confirmed by microscopic examination (Fig. 1 *A* and *B*). Phagocytosis was increased at serum dilutions that did not result in visible agglutination of red cells. There was also enhancement when the particles were treated with serum and washed before incubation with the phagocytes. The effect of antiserum was ascribed to specific antibody because (*a*) normal rabbit serum at 1:400 dilution was ineffective; (*b*) antiserum absorbed with sheep red cells lost its opsonizing activity, and (*c*) antiserum absorbed with horse red cells was as active as non-absorbed serum. These results are compatible with the report[5] that the amoeba phase of the slime mould *D. discoideum* grew on certain strains of *Salmonella* only when the bacteria were pretreated with specific antiserum; however, the extent of phagocytosis was not ascertained directly. The results obtained with antiserum could be duplicated with IgG or with IgM-rich fractions prepared on 'Sephadex G-200' by Dr V. Nussenzweig. Binding to macrophages of IgG-coated SE is inhibited by non-immune IgG and is reduced by digestion of IgG with pepsin[2]. Non-immune IgG (0.5 mg/ml.) had no effect on the uptake by amoebae of SE pretreated with antiserum. In addition, Fig. 2 shows that on a protein basis, intact or pepsin-digested IgG (ref. 6) had nearly the same stimulatory activity. Thus, while antibodies stimulated uptake of SE by amoebae, the organism does not seem to possess receptors for IgG comparable to those on macrophages.

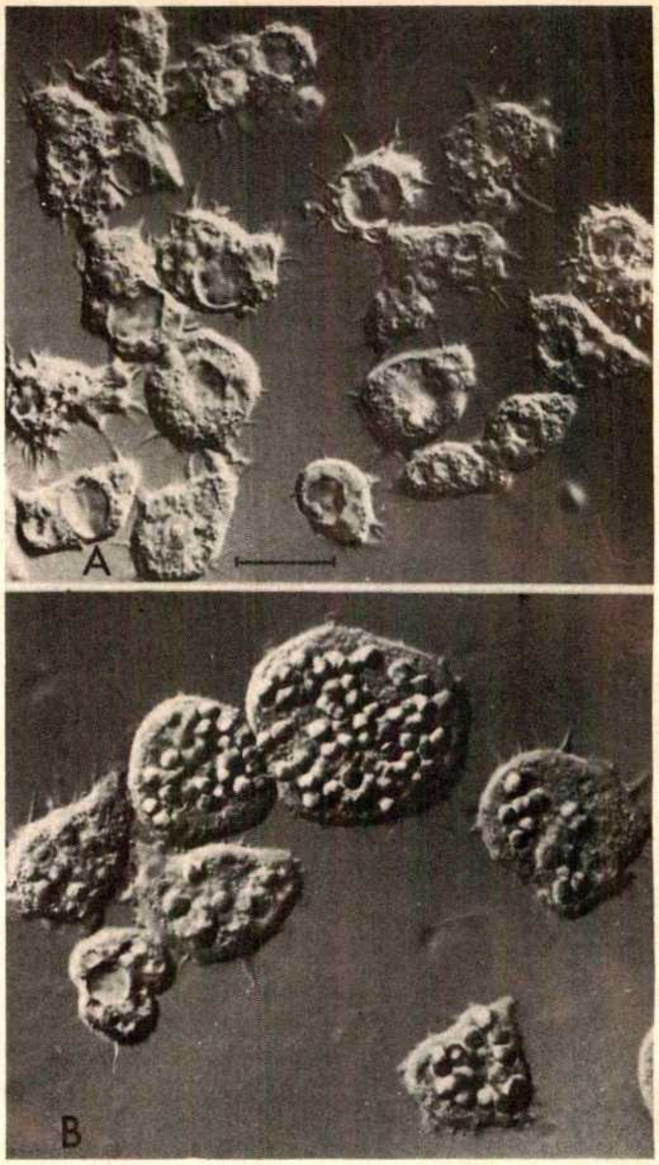

Fig. 1 *Acanthamoeba* incubated with sheep erythrocytes. Zeiss Nomarski optics. Scale line equals 20 nm. *A*, Control; *B*, 1:1,000 rabbit antiserum to sheep red cells was added to the amoeba-red cell mixture. Note absence of erythrocytes in *A* and extensive ingestion in *B*.

Plant agglutinins also increased the uptake of red cells. SE were treated for 60 min at room temperature, washed twice and incubated with amoeba. With Difco phytohaemagglutinins M (100 μg/ml.) or P (20 μg/ml.) or with concanavalin A (Miles) at 20 μg/ml., ingestion rates were, respectively, 0.0168, 0.0148 and 0.0113, whereas that of control red cells was 0.0001 units. A rate of 0.0030 was obtained when as little as 1.5 μg concanavalin A was added to 7×10^8 SE, or a maximum of about 18,000 molecules of agglutinin per SE (ref. 7). Amoebae pretreated with 10 μg/ml. concanavalin A, washed and incubated with SE, were ingested at rates similar to those of untreated amoebae, indicating that the agglutinin itself was not bound to the phagocytes.

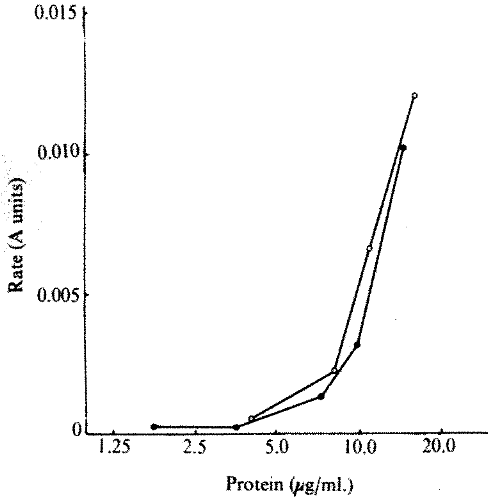

Fig. 2 Effect of control (closed circles) or of pepsin-treated IgG (open circles) on the ingestion of sheep red cells by *Acanthamoeba*. 0.5 ml. of the protein in saline-tricine was incubated with 3×10^8 sheep red cells for 30 min at room temperature; 10^6 amoebae in 0.5 ml. of saline-tricine was added per tube and the mixtures rotated at 22° C for 30 and 60 min. Non-ingested red cells were lysed, the amoeba pellets were washed and extracted with formic acid. Rates are (A 60 min—A 30 min)/30.

Several mechanisms could account for antibody or agglutinin stimulation of SE uptake by *Acanthamoeba*: (1) masking of antiphagocytic substances[8] that may be present on the SE surface; (2) addition to the SE of materials more likely to interact with the amoebae; (3) modification of the charge or other overall property of the SE in a way that favours particle-phagocyte interaction[9,10].

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Inhibition of Attraction and Cross-attraction by Interspecific Sex Pheromone Communication in Lepidoptera

MOST studies with lepidopteran sex pheromones have involved the stimulation or attraction of males by known chemicals or extracts of females, but chemicals which are responsible for inhibition of stimulation[1-4] or attraction[5-9] by an active pheromone may be equally useful. These inhibitory chemicals, which are often similar in structure to active pheromones, are effective either simultaneously or before the exposure of the insect to an active pheromone. We now describe a case in which male attraction to females of the same species is inhibited by a pheromone emitted from females of a closely related species.

Our tests were conducted with the Indian meal moth *Plodia interpunctella* (Hübner) and the almond moth *Cadra cautella* (Walker), both phycitid species. Non-mated 2-day-old males were released in closed 43 m³ rooms, under humidity and temperature control, 3 h before live non-mated 2-day-old females were introduced into small cages fitted inside traps constructed from quart-sized cylindrical paper cartons. A slow stream of air was directed through each trap, and 'Stikem' was coated inside the exhaust end of each trap-cylinder. The room was maintained on a 12:12 h light:dark cycle with the scotophase beginning 1 h after introduction of females. In one experiment we tested male attraction to females of each of the two species separately, and in another experiment to females of both species simultaneously. Whether used alone or in combination, fourteen females of each species were used in all tests. When used in combination, females of each species were held in separate traps to test the ability of males to select their own females. Individual tests of the two experiments were conducted alternately.

Our results (Table 1) reveal three distinct occurrences. (1) Indian meal moth males are attracted in equal numbers when only Indian meal moth females are present, only almond moth females are present, or when females of both species are present simultaneously. (2) Almond moth males are attracted to a degree similar to Indian meal moth males when only their own females are present. Almond moth males, however, are only slightly attracted to Indian meal moth females, and when females of both species are present simultaneously in comparison to female almond moths alone, there is a full 70% reduction in the total number of almond moth males attracted. (3) Most attracted males of each species select their own females, when given a choice of the two.

We eliminated visual selection by the males for their own females by installing baffles inside the traps to conceal the females. We also obtained similar selective attraction and inhibition of almond moth males when hexane–ether (1 : 1) homogenates of the abdominal tips of non-mated 2 day old females on filter paper were substituted for live females inside the traps. These results substantiate that chemical emission from females is the basis for selective attraction by both

Table 1 Effect of Female Moths of Other Species on the Attraction of Male Moths by Females of Their Own Species

	Average % ♂♂ attracted				
	Exposed separately		Exposed simultaneously		
Species ♂♂ tested	to AM ♀♀	to IMM ♀♀	to AM ♀♀	to IMM ♀♀	Total
AM	66±6	14±6	17±5	2±2	20±4
IMM	62±3	66±6	7±5	50±5	57±5

Average percentage attraction (±1 s.d.) of Indian meal moth (IMM) males and almond moth (AM) males after liberation in a 43 m³ closed room, in two types of experiments involving exposure to females of each species separately, and to females of both species simultaneously.

Results of forty-six individual tests. Total of 4,804 male moths tested.

males, and inhibition of almond male attraction by Indian meal moth females.

A component of the sex pheromone from females of both of these species has been isolated and identified as *cis*-9, *trans*-12, tetradecadien-1-yl acetate (I)[10,11]. This was the only sex stimulatory compound isolated from females of either species. Males of each species, however, are preferentially attracted to females of their own species when females of the other species are present. Further, almond moth male attraction is strongly inhibited in the presence of Indian meal moth females. We feel that these results can best be explained by the release of a multiple component sex pheromone from the Indian meal moth. On the other hand, Indian meal moth females may release relatively large amounts of compound I which is known to inhibit the stimulatory response of almond moth males[11]. Inhibition of attraction of almond moth males by compound I alone seems unlikely in these tests, however, because of the known small amount of this compound in the above inhibitory extracts of Indian meal moth females. These results along with previous results[11] indicate that females of both species emit multiple component pheromones which aid in isolating these species.

Clearly, this demonstration of a naturally occurring inhibition of attraction is significant to use of sex pheromones or pheromone components in the manipulation of insect populations.

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Pseudomonic Acid: an Antibiotic produced by *Pseudomonas fluorescens*

THE antagonistic effects of *Pseudomonas fluorescens* were first recorded by Garre[1] in 1887. Several reports since have dealt with the biological activity of cultures and extracts of *P. fluorescens*[2]. We wish to report the production and purification of these inhibitory substances and the characterization of a metabolite responsible for a significant proportion of the antibacterial activity.

A strain of *P. fluorescens* (a soil isolate, NCIB 10586) was grown in submerged culture at 30° C in a medium containing 1% corn steep liquor and 0.5% glucose in a basic salts solution. The maximum yield of the antibiotic occurred after 24 h and all detectable activity was in the culture fluid. (Activity was measured by the plate assay method using *Staphylococcus aureus* (NCTC 6571) as the test organism.) After the addition of barium chloride (0.5% w/v) the cells and precipitated non-active material were removed by centrifugation. The activity was progressively concentrated by partitioning into isobutylmethyl ketone (IBMK) (0.2 volume) at *p*H 4.5, water (0.8 volume) at *p*H 8.5, and then IBMK (0.25 volume) at *p*H 4.5, followed by evaporation to a small volume under reduced pressure. After a further partition into water at *p*H 8.5 and adjustment to *p*H 7–8, the aqueous solution was freeze dried to give a mixture of sodium salts which could be stored at 0° C for several months without loss of activity. Fermentations up to 3,000 l. have been routinely carried out, yielding 1–2 g sodium salts/100 l. culture fluid active at a concentration of approximately 0.1 μg/ml. by the plate assay method.

The antibiotic extract was stable within the range *p*H 4–9 at 37° C for 24 h. Outside these limits there was a significant loss of activity. The mixture of sodium salts showed a wide antibacterial spectrum against Gram positive and Gram negative bacteria, showed low toxicity and was bacteriostatic against *S. aureus* (NCTC 6571) and *E. coli* (MRE 600). It was haemolytic and inactivated by serum at concentrations $>50\%$.

The crude acid mixture was purified further by chromatography on 'Amberlite XAD-2' polystyrene resin with a linear gradient produced by adding 0.01 N methanolic ammonia to 0.01 N aqueous ammonia. A series of low molecular weight acids was eluted first followed by fractions (30–60% elution) that possessed the major part of the antibacterial (biological) activity. Reaction of these fractions with diazomethane yielded a mixture of methyl esters that could be separated into two fractions by thin-layer chromatography on silica gel (GF_{254}) on development with chloroform/isopropanol (9:1). The major fraction (R_F 0.4) crystallized from benzene/petroleum ether as colourless needles, melting point 76.5–78° C. Elemental analysis indicated the formula $C_{27}H_{46}O_9$ (found: C, 62.8; H, 8.9; $C_{27}H_{46}O_9$ requires C, 63.0; H, 9.0%), and the ester is optically active ($[\alpha]_D^{24}$ −9° (c, 1.5 in chloroform). Analysis of the oily *p*-bromophenacyl ester indicated a formula $C_{34}H_{49}BrO_{10}$ (found: C, 58.1; H, 6.9; $C_{34}H_{49}BrO_{10}$ requires C, 58.5; H, 7.0%). Thus the formula of the parent monocarboxylic acid, for which we propose the name pseudomonic acid, is $C_{26}H_{44}O_9$. Further support for this formula derived from the mass spectrum of the methyl ester which showed the expected molecular ion at *m/e* 514. The infrared spectrum of the methyl ester showed ν_{max} (CCl_4) 3,440 (hydroxyl), 1,740 (ester), 1,715 and 1,650 cm^{-1} (α,β-unsaturated ester). The ultraviolet spectrum, λ_{max} (EtOH) 221.5 nm (ε 13,400) confirms the presence of the α,β-unsaturated ester linkage. The nuclear magnetic resonance spectrum showed the presence of two secondary methyl groups (τ 9.09, 8.81), an olefinic methyl group (τ 7.84), a methoxyl group (τ 6.40) and an olefinic proton (τ 4.32).

Acetylation of the methyl ester with pyridine/acetic anhydride affords a triacetate $C_{33}H_{52}O_{12}$, which absorbs 1 mol of hydrogen giving a dihydro derivative $C_{33}H_{54}O_{12}$, on catalytic hydrogenation, showing only end absorption in the ultraviolet. Reduction of the methyl ester with $LiAlH_4$ in tetrahydrofuran afforded 1,9-dihydroxynonane, melting point 46°, *bis*-phenylcarbamate, melting point 168–9° (melting point[3] 42.5–44.5°; *bis*-phenylcarbamate, melting point[3] 171.5–172.5°). Treatment of the *p*-bromophenacyl ester with $KMnO_4/NaIO_4$ gave *p*-bromophenacyl-9-hydroxynonanoate, $C_{17}H_{23}BrO_4$, m.p. 77.5–78° (found: C, 55.1; H, 6.4; $C_{12}H_{23}BrO_4$ requires C, 55.0; H, 6.2%). Mild base hydrolysis of the methyl ester yielded methyl 9-hydroxynonanate (oil) $C_{10}H_{20}O_3$. Further confirmation of the presence of the 9-hydroxynonanoate unit in pseudomonic acid is provided by the mass spectrum of the methyl ester. Mass measurement of the fragment at *m/e* 327 gave 327.18059 ($C_{17}H_{27}O_6$ requires 327.18075) corresponding to the loss of $-O(CH_2)_8CO_2CH_3$ from the molecular ion.

Thus pseudomonic acid contains the biogenetically unique 9-hydroxynonanoic acid, the hydroxyl group of which is joined to the rest of the molecule through an α,β-unsaturated ester linkage. The structure of pseudomonic acid and other biologically active metabolites of *P. fluorescens* is under investigation.

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Infectious Pancreatic Necrosis in Rainbow Trout in Scotland

INFECTIOUS pancreatic necrosis (IPN), a highly contagious viral disease of young trout, endemic in wild salmonids and some trout farms in the United States, and first recorded in Europe in 1965[1], has now been positively identified as causing an epizootic of rainbow trout fry (*Salmo gairdneri*) in a Scottish trout farm during February and March this year.

The signs seen in this outbreak were typical[2], general dorsal darkening, swollen abdomen and the white mucous filling the stomach and intestine. Stained sections (haematoxylin and eosin) of the pyloric caecal area showed severe necrosis of the pancreatic tissue, which was well infiltrated with macrophages and in some cases almost completely degenerated. For electron microscopy, pancreatic tissue from diseased rainbow trout was fixed in osmium tetroxide in veronal buffer[3], dehydrated through an ethyl alcohol gradient and embedded in 'Araldite'. Ultrathin sections were cut on an LKB Ultrotome III using glass knives and mounted on uncoated grids. They were stained by the alkaline lead oxide method[4] and examined in a Siemens Elmiskop I using the double condenser system and an accelerating voltage of 60 kV. IPN virus particles were found, both distributed randomly in the cell cytoplasm and in cells with areas of necrosis, in membrane-bound aggregates 1–3 μm in diameter (Fig. 1). The virus particles were hexagonal in profile, averaging 55 nm in diameter and, in some membrane-bound aggregates, arranged in crystalline arrays[5,6] (Fig. 2).

The virus was isolated in 1–3 day-old RTG2 (rainbow trout gonad) and FHM (fat head minnow) cell lines kept at 20° C and infected with filtered (0.22 μm 'Millipore') complete fish homogenates of distressed fish (diluted to about 1 : 50 in Hanks BSS). The isolate has been passaged several times.

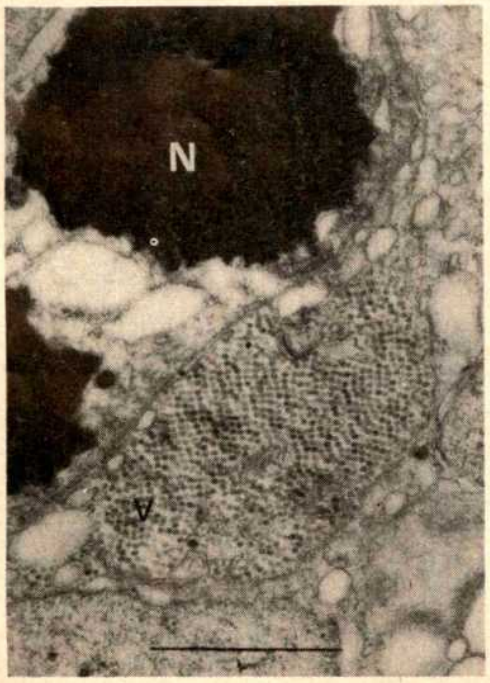

Fig. 1 Electron micrograph of ultrathin section of rainbow trout pancreatic tissue. Part of a cell showing necrotic area (N) and viral inclusion (V). Marker, 1 μm.

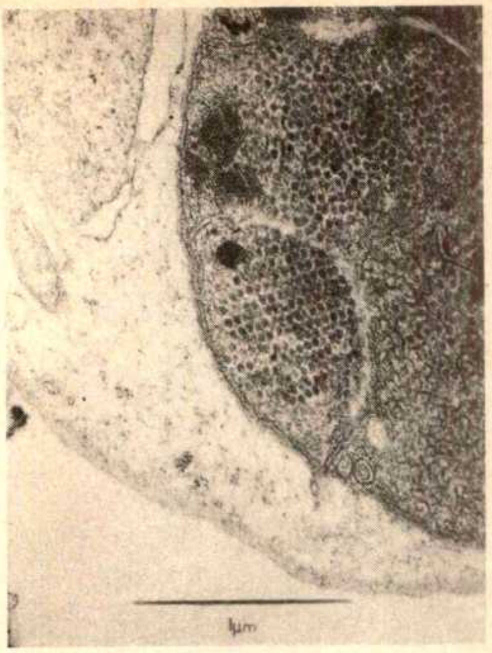

Fig. 2 Electron micrograph of an ultrathin section of rainbow trout pancreas. IPN virus particles showing early stages of crystal lattice formation. Marker, 1 μm.

Supernatant cell culture fluid from the fifth passage was added to water containing sea trout fry (*Salmo trutta*) which had just commenced feeding. Fry mortality with most of the gross pathological signs were noted from the sixth day, pancreatic necrosis was confirmed in sections and the virus was isolated in RTG2 cells from moribund whole fish.

Characterization of the virus as IPN included a serum neutralization test using goat anti-IPN serum (Microbiological Associates, Inc.). This serum is specific for strain VR299 (American Type Culture Collection) of IPN virus; it delayed the occurrence of a cytopathic effect in RTG2 cells but did not prevent it. Survival in 10% ether and 50% glycerol (the latter for 1 month) was demonstrated[7].

The farm where this outbreak occurred is comparatively new and has received only four shipments of eggs, all from one supplier in Denmark. The disease occurred in fry hatched from the second shipment which arrived in late September 1970 and which started to feed in late January. Mortalities were noted in increasing numbers from mid-February onwards. These events implicate the eggs as the means of transmission of the virus as has been suggested by others[8]. It is interesting to note that this early winter spawning strain, which was introduced from France and America, is thought to be the origin of IPN in Denmark[9].

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Syntactic Class as a Determinant of Word-retrieval in Normal and Dyslexic Subjects

SUBJECTS with dyslexia following brain lesions may read concrete nouns significantly better than other parts of speech[1]. There may be a normal analogue in tachistoscopic recognition thresholds for different parts of speech. The only study in which this has been investigated[2], however, was conducted with German adolescents, and the results may have been biased by a difference in the relative usage of concrete nouns by adolescents and adults.

We have conducted similar experiments on syntactic class effects in English, and have investigated the reading performance, on the same material, of a small group of subjects with residual acquired dyslexia. A list of sixty words, consisting of twenty concrete nouns, twenty adjectives and twenty verbs, was used. The words vary in length between four and seven letters, and are divided into five frequency ranges (Thorndike and Lorge[3]). All words are matched for length and frequency across the three syntactic classes; there are equal numbers of words in all frequency ranges and at all lengths.

In the first experiment, these stimuli, typed in lower case (Delegate typeface) letters, were presented individually in a three-channel tachistoscope (Scientific Prototype, MFG Corp, model GB). The subject fixated a central cross in the pre-exposure field, and, after a "ready" signal, the stimulus was presented centrally, followed by a blank post-exposure field. An ascending method of limits was used; the first exposure was 10 ms and on each successive exposure the duration was increased by 5 ms until the subject correctly reported the stimulus on two consecutive trials. Order of presentation of the sixty stimuli was randomized anew for each subject. Practice trials were given to familiarize the subject with his task. The subjects were twenty students, technical and academic staff of the University of Edinburgh (mean age 24 yr). The results are shown in Table 1. Friedman two-way analysis of variance shows that the effects of syntactic class, length and frequency are significant at beyond the 0.001 level. The difference between nouns and verbs is significant (Wilcoxon matched-pairs signed-ranks test, $T = 2$; $P < 0.001$, two-tailed), as is the difference between nouns and adjectives ($T = 40.5$; $P < 0.02$, two-tailed) and adjectives and verbs ($T = 27$; $P < 0.01$, two-tailed).

To check that these results are not due to uncontrolled (and at present uncontrollable) variation in the purely visual properties of the stimuli, a second experiment was conducted using the same words in upper case (Delegate) letters. Seven subjects from the same population as before (mean age 20 yr) were tested. The initial exposure was 10 ms, increasing by 10 ms on each trial. In all other respects, the experimental method was the same as in experiment 1. The mean recognition thresholds for the syntactic classes were: nouns, 37.0 ms; adjectives, 41.4 ms; verbs, 45.2 ms. Friedman two-way analysis of variance shows that these values are not drawn from the same population ($Xr^2 = 7.36$; $P < 0.05$). The difference between nouns and verbs is significant at the 0.05 level ($T = 0$). With such a small number of subjects, the noun/adjective and the adjective/verb differences fail to reach significance. The upper case means are higher than lower case, as is customarily found, but the effect of syntactic class is still demonstrable.

Table 1 Mean Recognition Thresholds in Milliseconds

						Xr^2
Syntactic class	Nouns 30.3	Adjectives 33.3	Verbs 35.8			21.63*
Length (in letters)	Four 39.5	Five 31.7	Six 32.1	Seven 29.9		57.8*
Frequency	AA 27.5	A 27.1	37–17 30.0	18–8 39.4	8–1 41.6	40.9*

* $P < 0.001$.

The same words, in lower case, were presented for reading aloud, to five dyslexic subjects, mean age 48 yr. All five men received penetrating missile injuries to the left hemisphere during the Second World War. All have residual language impairment with a disorder of reading being one of the predominant features (for further details of these cases, see Marshall and Newcombe[4]). The words were presented, individually typed, on plain white cards. No time pressure was imposed. The subjects read correctly eighty-one nouns (out of 100; twenty nouns, five subjects), fifty-five adjectives and fifty-four verbs ($Xr^2 = 6.3$; $P < 0.05$). The effects of length and frequency are significant at beyond the 0.01 level. Thus a number of stimulus variables which affect tachistoscopic recognition thresholds are also correlated with dyslexic performance.

The order of difficulty in syntactic class (verb > noun) and over the frequency ranges (infrequent > frequent) is the same in both the dyslexic and the normal subjects; but increasing length (between four and seven letters), which is correlated with a lowering of threshold in the normal subjects, resulted in increased difficulty for the dyslexic subjects. A further difference is that thresholds for adjectives for the normal subjects are intermediate between nouns and verbs, while for the dyslexic subjects reading-performance on adjectives is indistinguishable from that on verbs. (Halpern[1] has also reported this latter result.)

The next task is to discover how and why the observed facilitation of nouns takes place.

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Lateral Thinking about Lateral Inhibition

IT has recently been asserted[1] that the well known apparent expansion of acute angles is due not to the lateral inhibition proposed by Blakemore *et al.*[2], but to an adaptation effect similar to the Gibson tilt after-effect[3,4]. The arguments by which Coltheart arrives at this conclusion, however, seem to us to be based on a complete misreading, and hence misrepresentation, of our article, which we should like to correct.

The strongest reason for rejecting adaptation as an explanation for angle expansion is, as Coltheart correctly adduces, the fact that disinhibition (that is, partial cancellation of angle expansion) may be produced by introducing a third line into the figure. Coltheart proceeds to discuss the special case in which the disinhibiting line lies outside the angle in question, and states, again correctly, that both adaptation and inhibition would reduce the degree of apparent expansion. He does not consider the more informative and critical case where the disturbing line lies inside the angle. Here, adaptation and disinhibition predict exactly opposite effects. Our own experiments show that disinhibition occurs equally strongly whether the third line is inside or outside the angle; it is for this reason, primarily, that we reject the adaptational explanation.

In any case, Coltheart's argument assumes that it was the apparent size of the angle as a whole that was measured. Our paper makes it perfectly clear that our observations were on the apparent orientation of the arm of the angle further from the third line, and not on either the nearer arm or the angle as a whole. His argument is therefore fallacious as well as incomplete.

Coltheart comments unfavourably on the difference between the usual angular distributions of inhibition commonly obtained in orientation-masking studies, and our Fig. 1 (ref. 2), but this figure does not, as he seems to suppose, represent the spread of inhibition from a single line, but rather the total pattern of activity, combining both excitation and inhibition, which both fall off monotonically from the optimal orientation, as is stated explicitly in our paper: the trough at 6° occurs because the excitation falls off more rapidly than the inhibition, and has nothing to do with maximal inhibition or maximal masking. There is therefore no discrepancy to explain.

Finally, we are at least grateful to Coltheart for pointing out the remarkable similarities between the simultaneous angle expansion and the successive tilt after-effect. Their magnitudes, directions, and even their time-courses are similar. This leads us now to propose that far from the simultaneous effect being due to some ill-defined "adaptation" or "satiation" of orientation detectors, the Gibson after-effect itself may be due to the long-lasting consequences of prolonged inhibition. Adaptation may be due to lateral inhibition, but certainly not the reverse.

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Paradox with After Images

A few years ago, experimenting with the crisp after images that are left by an electronic flash, I noticed something which surprised me since it seemed to contradict views about after images in relation to dark adaptation.

Only recently have I seen that some very obvious considerations resolve the paradox, and the "surprising feature" is just what common sense should have led one to expect. Though I confess it has taken me a long time to see the obvious, I have little doubt that many readers will see it as soon as they try. Therefore this week I present the paradoxical observations; the week after next I shall give experiments to support the rather obvious resolution.

To make the paradoxical observation the eye is bleached by an electronic flash presented in Maxwellian view (Fig. 1*a*). The flash tube is at the focus of lens L_2 and the subject's pupil at the focus of lens L_1. In the collimated region between L_1 and L_2 is a circular aperture (Fig. 1*b*) divided into three regions by the interposition of neutral densities meeting at lines set at 120° with each other, the densities being 0.0, 0.2 and 0.5. The demarcation lines are seen sharply, and after discharging the flash they are at once conspicuous in the cone after image which follows. Ten minutes later the cone image has faded beyond recall, but the grey rod after image may be recalled for a further 15 min.

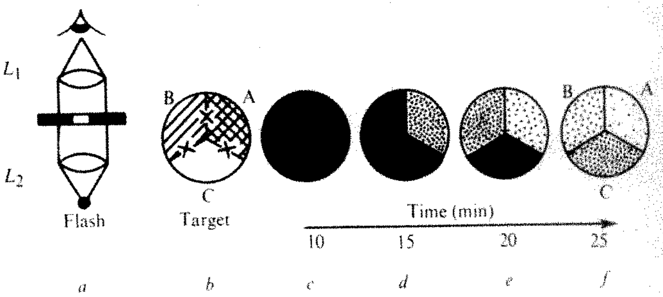

Fig. 1 *a*, Electronic flash collimated by lens L_2 and presented to eye in Maxwellian view by L_1. Interposed mid-way is the tripartite filter shown in *b*. Sectors A, B, C are neutral densities 0.5, 0.2, 0.0 respectively. The centre is fixated and areas A, B, C of retinal image differently bleached. *c*–*f* represent the appearance of the negative after image seen by momentarily opening the bleached eye and viewing a faintly illuminated white wall. At 10 min (*c*) the image is uniformly black; at the subsequent times shown, it breaks up into sectors and gradually fades in blackness.

A good way to recall after images is to blink in a room dimly lit. When the eyes are shut we see a positive after image, which is a faint replica of what was seen during the flash. When the eyes are opened we see against the white wall a negative after image, the same picture as the positive but with contrast reversed like a photographic negative. In my experiment the eyes were kept shut and opened for a second or so from time to time, and the negative after image was thus seen against the white wall.

The surprise is that the proper negative of Fig. 1*b* is not seen until Fig. 1*e*, 18 min after the flash. At 10 min all we see is a black uniform circular patch without subdivision. At 15 min suddenly a lighter portion separates out (Fig. 1*d*) corresponding to the retinal region bleached through 0.5 filter, and this portion continues to get lighter and lighter, the black part remaining unchanged. At about 18 min suddenly the black part shows a demarcation line (Fig. 1*e*) and the region bleached through the 0.2 filter starts to get lighter. Finally the most strongly bleached retina slowly pales and the rod after image finally fades away.

If we consider these changes in reversed time, going from (*f*) to (*e*) of Fig. 1, all three sectors get darker as pigment regeneration is less advanced. But evidently the intensity of after image does not increase indefinitely. In each sector there is a fixed ceiling of intensity above which the image cannot go. The lowest sector (C) is most bleached, and hence is first to reach the ceiling (going backwards in time). By Fig. 1*d* sector B has also reached the ceiling, and at 10 s (Fig. 1*c*) the whole area is at the same ceiling level.

Now Barlow and Sparrock[1] showed that at every stage in dark adaptation, the log threshold for test flash detection (the ordinary dark adaptation curve) is raised in proportion to the log brightness of the after image, which they claim is the immediate cause of the familiar desensitization by bleaching. If there is a ceiling to the intensity of the negative after image, either there must be a corresponding plateau in the rod dark adaptation curve, or else this image intensity cannot be the cause of the threshold rise. Fig. 2 shows dark adaptation curves in the experiment which gave the images of Fig. 1. There were three small red fixation points set in an equilateral triangle and the small test flash fell at its centre. When immediately after the bleaching flash I went into the dark adaptometer and fixated on the centre, I saw the positive (cone) after image and the three fixation points at the places marked by crosses on the radii, Fig. 1*b*. Thus fixating in turn on each red light permits the test flash to fall in the middle of the three bleached regions. Fig. 2 shows the three rod dark adaptation curves each preceded

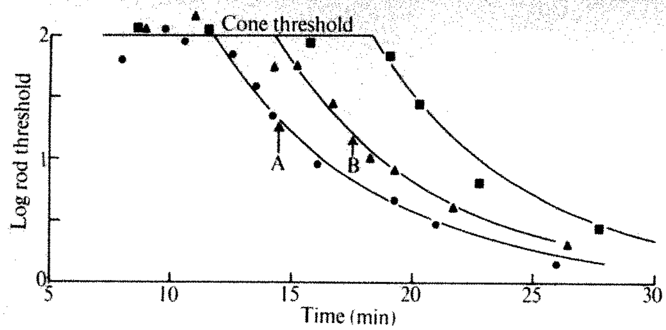

Fig. 2 Dark adaptation curves, that is, log threshold for test flashes plotted against time after the bleaching flash. Curves A, B, C plot measurements when the test fell near the middle of bleached areas A, B, C respectively of Fig. 1*b*. Curves drawn through rod branches are the exponential with half decay time of 4.5 min. Arrows A, B mark the moment when the appearance of the after image changed from Fig. 1*c–d* and *d–e*, respectively.

by a cone branch. They are normal rod curves, each being an exponential that falls to half in 4.5 min. The vertical arrows A, B indicate the moments when sector A separated itself (Fig. 1*d*) and segment B separated (Fig. 1*e*).

It is plain from Fig. 2 that the arrows, which mark the ceiling of after image intensity, correspond to a fixed ordinate in the dark adaptation curve, a fixed threshold rise above the full dark value. But it does not correspond to any flattening or ceiling of threshold rise. If Barlow and Sparrock[1] were correct in saying that the intensity of our after image was the immediate cause of the threshold rise, how could thresholds continue to rise to the left of the arrow in Fig. 2 though the after image remains unchanged in intensity?

I think many readers will be able to answer this. The week after next I shall give experimental confirmation of what they probably expect.

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Conservation of Water-damaged Written Documents by Freeze-drying

ECONOMIC considerations generally eliminate freeze-drying as a practical method for the drying of paper materials. Although we are aware of accounts in the literature about the freeze-drying of paper materials (generally filter paper) we have not seen any references to work on the freeze-drying of written documents for conservation purposes.

While a fire was being extinguished at the Greenland Regional Library in Godthåb during the winter of 1968, many valuable items (hand-written manuscripts, books, letters and so on) became wet and subsequently froze. The damaged items were transported in their frozen state to Copenhagen and held there for 2 yr while a decision was made about the drying method to be adopted. Most of the printed books were air-dried in the conventional manner, with good results considering the circumstances.

The more valuable items were hand-written letters, manuscripts and maps belonging to a mid-nineteenth century missionary to Greenland, Samuel Kleinschmidt. It was felt that the ink used in these documents would run during the melting associated with an air-drying process, thus ruining them. Our laboratory was therefore asked to undertake the freeze-dehydration of the frozen written materials.

Some preliminary experiments with modern papers and writing materials were conducted to gain some experience in handling frozen hand-written materials. These experiments showed that temperatures up to at least 110° C can be tolerated for several hours without discoloration of the paper. The advantage of freeze-drying was made clear by a comparison experiment in which paper marked with various modern writing materials (ink, ballpoint pen, felt-tip marking pen) was immersed in water, frozen and then dried. The freeze-dried sample was perfect, whereas the writing on the air-dried sample had run.

The twenty-seven storage packets in the Kleinschmidt collection and a photograph album were transported from the Copenhagen branch of the Greenland Regional Library to the Food Technology Laboratory in insulated containers cooled with dry ice. The papers were held at −30° C until prepared for freeze-drying. The storage packets were tight fitting paper and cardboard holders of the standard type used in libraries for filing loose papers. A preliminary trial showed that, by careful manipulation of the frozen packets, these holders could easily be removed thus eliminating a large resistance to mass transfer in the packet. Both to facilitate the rate of drying and to ensure sufficient clearance between the heater shelves, some packets had to be prised apart while frozen. This was made easier by the fact that the packets consisted of groups of paper folders. Stacks of the prepared frozen papers 2 to 3 cm thick, were placed on pre-cooled, porous sample trays and conservative freeze-drying conditions were chosen so that no melting or colour change could occur. Radiant heating at a plate temperature of 45° C and a chamber pressure of 200 mtorr was used. The sample weight was monitored using the balance built into the freeze-dryer (Atlas Ray 1) and drying was continued to constant weight. The average drying time in these conditions was about 1.5 to 2 days and when the drying was complete, the chamber vacuum was slowly released.

The drying process gave perfect results for all the written paper documents. Each page separated easily and in no case did the ink run. A few of the envelopes were stuck together as some of the old wax seals had softened (probably due to the use of the elevated heating temperature). They separated on cooling though some transfer of the wax colour had occurred. It was observed that packets (usually the thicker notebooks) which had been compressed into certain shapes before freezing retained the principal features of that shape after drying; and because of the pressures which developed there was a tendency for the packets to expand like an accordion as they dried. These misshapen samples were later treated in the usual manner of pressing and rebinding.

The photograph album presented more problems, the most serious of which was the tendency of those prints which were frozen emulsion to emulsion, to stick together after drying. Whenever possible, the groups of dried prints that were stuck together were removed from the album, soaked in water and then carefully pulled apart under water. This was usually successful, although in a few cases small portions of the pictures were destroyed. An ordinary darkroom photoprint dryer was used for drying of the separated prints.

The thickness of the photoalbum (10 cm) demanded freeze-drying for 4.5 days. This time was, however, found to be slightly too short, for a group of six pictures located on the centre page was still frozen together at that time. They unfortunately melted before they could be reinserted into the freeze-dryer, ruining the ink hand-written captions. This showed that freeze-drying had indeed been necessary to successfully conserve the written documents.

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BOOK REVIEWS

Cells and Cancer

The Cell Cycle and Cancer. Edited by Renato Baserga. Pp. xii+481. (Marcel Dekker: New York, June 1971.) $29.50.

I DO not recollect having previously reviewed a scientific book on a topical subject which carried on its jacket a reproduction of a Renaissance painting. The departure in this instance may reflect the tastes of Dr Baserga, whose own contributions to the volume are liberally sprinkled with classical allusions. The editor's imprint on this volume is unusual in another respect in that, instead of writing a formal introductory chapter, he has interspersed the twelve chapters with explanatory and introductory sections. This practice, which Dr Baserga attributes to one of his teachers, might well be copied by editors of other symposium volumes. The reason for these connecting sections, of course, is to try to link together the chapters written in different styles by different authors. In fact, this particular book concentrates on one relatively small topic and, therefore, is quite coherent. Indeed its principal shortcoming is that there is a fair amount of overlap in it; for example, the labelled mitosis method for studying the cell cycle is described many times. This repetitiveness, which may be unavoidable in a volume of this kind, is the chief criticism one can make of it.

The book contains twelve excellent essays on different aspects of the cell cycle, which among them provide an almost complete review of the subject. The first three chapters, by Lipkin, Blackett and Mendelson and Takahashi, are concerned with mathematical aspects of cell cycle kinetics. The next three chapters are concerned with the cell cycle in different normal and diseased states. The cell cycle in cancer cells is discussed by Gavosto and Pileri, in differentiation by Malamud and in response to hormones in different organs by Epifinova. The next four chapters are concerned chiefly with biochemical aspects of the cell cycle. Cooper discusses biochemical alterations accompanying the initiation of growth; Vendrely, cytophotometry and histochemistry in the cell cycle; Mueller, biochemical aspects of the G1 and S intervals; and Tobey, Petersen and Anderson, the biochemistry of G2 and mitosis. Most of the first ten chapters are devoted to reviewing material, much of which has previously appeared in other books. The eleventh chapter, by Skipper, on the cell cycle and chemotherapy of cancer, is refreshing in that it not only analyses this topic, but also introduces some new ideas about it. The final chapter, on radiobiology and the cell cycle, by Frindel and Tubiana is an excellent, comprehensive review of this large and complex subject.

This is a first rate source book for people working on aspects of the cell cycle. Most of the discussion is at a fairly advanced level and the views expressed seem generally sound. I would take issue with only one or two points (both of those mentioned voiced by the editor). Is it really true that the theory of contact inhibition has been demolished and, by implication, has nothing to contribute to the understanding of cancer (page 55)? Is there justification for suggesting that the differential effects of hydroxyurea on cells in S phase and in G0 may indicate both a metabolic diversity between G0 and G1 cells and that the S phase may be different in different cells (page 191)?

What general impression does one gain about the field by reading this book? My impression is that, although an enormous amount of work of very high quality has been done, we are only a little further forward in the understanding of the mechanism of the cell cycle than we were in 1963 when Howard and Pelc described it. What we have perhaps come to appreciate is the great complexity of the problems. The reproduction on the front cover is of Raphael's St George and the Dragon. St George's allegorical identity is obscure but I imagine the dragon represents the cancer problem. Is the maiden praying for divine intervention in the background possibly intended to represent scientists engaged in studies of the cell cycle?

JOHN PAUL

Receptor Physiology

Principles of Receptor Physiology. Edited by W. R. Lowenstein. Pp. xii+600. (Springer-Verlag: Berlin and New York, 1971.) 134.40 DM; $37.

The Handbook of Receptor Physiology, to be compiled in eight sections, of which this volume is the first, will represent a major achievement in the literature of physiology.

The ability of the cell or organism to perceive, analyse and react to external stimuli is clearly one of the most important functions of living systems: in particular, the property of chemosensitivity must have been of early evolutionary significance. The wide variety of incoming stimuli has necessitated the development of a large number of sensory receptors, all of which serve directly or indirectly to transduce the incoming stimuli into trains of sensory impulses, a common output, a fact recognized by Adrian almost fifty years ago and expressed in the frequency code hypothesis. The various transducing mechanisms pose a well recognized and inspiring challenge to which workers in many disciplines are responding with vigour. Unquestionably, more remains to be learnt than has been learnt hitherto and as Ottoson and Shepherd (chapter 15) note for the well investigated muscle spindle, "the basic questions underlying the transducer process are still kept by the spindle as a well guarded secret of its own". The exquisite sensitivity of many transducer mechanisms (insect sex pheromones, reptilian heat receptors) poses the additional question of what molecular gyrations can be responsible for detecting and responding to such low level stimuli? The wide range of input stimuli to which the sensory systems react poses another severe challenge to the understanding of these input–output systems.

This volume is designed to serve as an introduction to receptor physiology by introducing a selection of topics, some of which will be covered in greater detail in subsequent volumes, and which are intended to introduce and survey the field of receptor physiology. This volume includes seventeen chapters dealing with general characteristics of excitable cells, mechanochemical transducers, light perception mechanisms, the analysis of stimulus intensity and peripheral receptor organization. Nachmanson's chapter deals with the roles of the proteins of the acetylcholine receptor in transducing bioelectric events: it contains much useful information on the fruitful applications by Changeux and others of the allosterism concept to chemically sensitive membranes. Yet much of the chapter is devoted to a further restatement of Nachmanson's views on the general role of acetylcholine in nerve impulse propagation. This particular controversy is too well known to require additional comment here. The immediately subsequent chapters (Tauc and Grundfest) deal with chemical transmitter action in a number of excitable systems and, in typically clear fashion by Grundfest, with the general electrophysiology of the specialized input membrane in excitable cells.

The general relationships between sensory intensity and stimulus analysis are well dealt with by Lipetz and Stevens; the latter presents a stimulating discussion of the Weber–Fechner hypothesis and more recent power function analyses to correlate sensory intensity analyses. Two chapters deal with visual perception: that by Cone and Pak deals very adequately with the origin of and basis of the early receptor potential and Feinleib and Curry discuss phototaxis in plants. As these authors note, the phototactic system may represent a very simple receptor–effector relationship which is, despite past failures, well suited for a complete input and output analysis. The recent discovery of retinal bound to an opsin-like protein in *Halobacterium holobium* (D. Oesterhelt and W. Stoeckenius, *Nature New Biology*, **233**, 149; 1971) and its similar orientation in the membrane (A. E. Blaurock and W. Stoeckenius, *Nature New Biology*, **233**, 152; 1971) to that in vertebrate retinas suggests the validity of examining simpler biological systems.

I have one major criticism of this book: in a series of topics all of which relate to the cell membrane in some respect it seems an oversight not to have included a specific chapter on the structure and function of cell membranes. There are a number of minor misprints but these do not detract from the high quality of the book. Its price is unfortunately too high to place it in the hands of many individuals. This is a pity, for the book deserves wide circulation. It is an excellent introduction to the proposed series and editors and authors alike are to be congratulated. Subsequent volumes will be eagerly anticipated. D. J. TRIGGLE

Biochemical Evolution

Biochemical Evolution and the Origin of Life. Edited by E. Schoffeniels. (Proceedings of the International Conference on Biochemical Evolution.) (Molecular Evolution II.) Pp. xiv+398. (North-Holland: Amsterdam and London, 1971.) £8.40.

THIS volume contains papers on a variety of topics in speculative and comparative biochemistry. They range from careful statistical studies of the rate of evolution of protein sequences to highly speculative histories, for example of the evolution of metabolic pathways. Some of the papers are excellent, but others are of doubtful value; they provide a good sampling of the field, both with respect to subject matter and quality.

It is clear that the students of protein sequences have many more data on which to base their theories than those who work on other branches of biochemical evolution. The paper by Margoliash, Fitch and Dickerson provides a definitive summary of the conclusions that can be drawn from the extensive series of cytochrome c sequences that have been determined so far. Other interesting papers deal with fibrinogen and immunoglobulin sequences.

The evolutionary biochemistry of small molecules is a much more difficult subject. However, it is at least as interesting, since it provides the only hope of understanding evolution in the period before the major outlines of biochemistry became fixed. Unfortunately, the law of pure cussedness applies in this area: the more primitive the process, the more difficult it is to say anything definite about its evolution. The phosphagens and phosphagen kinases must be comparative newcomers to the biological scene; Watt's discussion of the subject is fairly convincing. Energy production, on the other hand, must be a very primitive process; Broda's interesting treatment of bioenergetic evolution raises as many questions as it answers.

The expert will encounter some new material in this book and much that he has seen before. The general reader should find it a useful introduction to the subject. L. E. ORGEL

Biochemical Text

Cellular Biochemistry and Physiology. By N. A. Edwards and K. A. Hassall. Pp. xiv+442. McGraw-Hill: Berkshire, September 1971.) £3.95.

I REMEMBER a friend who was a physicist telling me that his initial test of the value of a dictionary was to look up the entry for "entropy". As might be expected, I tend to look first at the preface of a textbook of biochemistry and then at the chapter on the biosynthesis of proteins.

In the case of the present book I followed this scheme with rather disastrous results. I was with the authors so far as their aim was concerned, for I am sure that many students like their biochemistry to be based on cell physiology and ultrastructure. The chapter entitled "Polynucleotides and Protein Synthesis" is, however, an awful mess and makes one wonder whether the authors really understand their subject. A typical statement is (page 346): "Under normal conditions, ribosomes not aggregated in this way make little or no protein although, in the presence of an excess of messenger RNA, single ribosomes synthesize protein quite adequately". Their explanations of the structure of DNA and RNA, the way in which Kornberg polymerase effects the synthesis of DNA, and the steps in the attachment of amino-acid to tRNA, to mention just a few points, are very confusing. It really hurts to see such a beautiful story spoilt in this way.

The first chapter on the cellular basis of life would hardly encourage a student to read on, but if he did he would get to proteins, peptides and amino-acids. There is an amazing diagram showing amino-acids hanging from a thread followed by Table 2–1 giving tests for amino-acids (Sakaguchi, Millon and so on). The latter is just the kind of material the authors promised to exclude. The major considerations that led to the concept of the α-helix are not mentioned and Fig. 2–8 is original but not helpful. Do we really have to *speculate* that the tertiary structure of a protein is the inevitable consequence of the primary structure?

In the chapter on mitochondrial electron transport and oxidative phosphorylation, instead of explaining the objective of the whole business, followed by redox potentials, these matters are left to be described relatively late in the chapter. What happened to "fumarate" in Fig. 6–1? The book ends with a "systematic classification of enzymes" and a very poor list of references.

The authors had a worthwhile objective but in my view they have failed. The book is not to be recommended to students, but we need not be too unduly worried, for it seems very unlikely that a student wanting an elementary text would pay £3.95.

P. N. CAMPBELL

Estuarine Ecology

Ecology of Estuaries. By Donald S. McLusky. Pp. viii+144+8 plates. (Heinemann: London, October 1971.) £1.60.

ESTUARIES are complex and variable environments. A recent symposium on estuaries held in America resulted in a volume containing more than 700 pages, with little overlap in the subject material of the various authors. In a book aimed at sixth formers and first year university students, Dr McLusky has made a brave attempt to provide a concise account of the ecology of estuaries in less than 150 pages. I think he has succeeded. The style is clear, and the general principles of estuarine ecology are well explained, but condensation has meant oversimplification to the point of error in some places. Estuarine plants are dealt with in four pages, and it is implied that there is a simple gradient of water logging in salt marshes. In fact one frequently finds that the *Juncus* zone at the top of the marsh is more water logged than the middle zones, so that algae present on the lowest part of the marsh reappear on the upper marsh, although absent from the middle.

In general the information in the book is accurate, but there are a few errors. The diagram of the burrow of *Arenicola* shows a simple U-tube open at both ends, and on page 40 it is stated that *Nereis diversicolor* appears to avoid low salinity regions.

References in the text are always a problem in a book of this type, and their use in the present volume is erratic. No references are given in the text of the chapter on plants, but a considerable number are given in the chapter on animals. A point which I found disturbing was the attribution of some figures to secondary sources rather than to the primary ones. For example, Fig. 14 is attributed to Kinne, but Kinne correctly attributes it to Pantin; Fig. 16 is attributed to Lockwood, but Lockwood himself correctly attributes it to Ellis. Even in the text at one point the well known work of Wells on the oesophageal pacemaker of *Arenicola* is attributed to a secondary source. These points are probably more important to the advanced reader who likes to know who actually did the work.

In spite of these criticisms of details the book will be most useful as a first introduction to the ecology of estuaries.

J. GREEN

Hydrides

Hydrides of the Elements of Main Groups I–IV. By E. Wiberg and E. Amberger. Pp. xv+785. (Elsevier: Amsterdam, New York and London, September 1971.) Dfl. 290.00; £33.85; $80.75.

THIS is a scholarly and comprehensive monograph which provides a detailed and reliable source of information on all aspects of the chemistry of the hydrides of the elements in main groups I–IV. The authors are internationally respected authorities in this field and their coverage of over 3,500 original references extends to 1970.

The book is extremely well organized and the skilful use of diagrams and tables enables a tremendous amount of factual information to be recorded while leaving the cursive text free to develop the significance of the data. Only in the introductory chapter (twelve pages) does this approach fail—the compression here is so great that the general review of hydride chemistry, the presentation of theoretical models of hydrides and the general summary of preparative procedures are less informative than many accounts in undergraduate textbooks.

The unique feature of the book is the extensive and perceptive discussion of the chemistry of the hydrides; there is a depth of understanding and insight here which is a welcome change from the approach in many recent books. Too often these days there is an apparent belief that inorganic chemistry begins and ends with a description of the spectroscopic and structural properties of complexes, and little regard is paid to the synthesis, reactions and reactivity of the compounds being discussed. It is refreshing to see some chemical chemistry again.

Two chapters deal successively with the hydrides of the alkali metals (30 pages) and the alkaline earth metals (38 pages). Each starts with a brief historical introduction and general review of the group, followed by a detailed discussion of the preparation, physical properties and chemical reactions of the hydrides of the individual elements.

The most extensive chapter (274 pages) concerns the boron hydrides. These compounds and their derivatives have been much reviewed in recent years but this new approach to their chemistry adds a new dimension to the literature on the subject which undoubtedly enhances our understanding of their subtle and intricate chemistry. Some 170 pages are devoted to synthesis, conversions, reactions and mechanistic schemes and this is followed by extensive tabulation of the physical properties of the boranes and their derivatives (sixty pages) and a bibliography, classified by compound, of references to infrared, raman, nuclear magnetic resonance, ultraviolet, microwave, electron spin resonance and mass spectra, and to structural determinations and molecular orbital calculations (thirty-five pages). A brief section on carboranes is also included in each section and, in all, 1,400 references are cited.

A similar approach is adopted in subsequent chapters, the length of each reflecting the amount of work published: aluminium hydrides (sixty-two pages), other group III hydrides (nineteen pages), silanes (177 pages), germanes (eighty pages), stannanes (thirty-eight pages) and plumbanes (eight pages). There is also an appendix (keyed to the main chapters) reviewing the work which appeared in some 150 papers during the early part of 1970.

Throughout the book the diagrams are a particularly pleasing feature and they enhance the text considerably. The style of writing is impeccable and great attention has also been paid to the general format, display of equations and clarity of print. Indeed the book is beautifully produced except for one ghastly mistake: in the review copy at least, pages 673–688 were missing and pages 641–656 were bound in twice. It is also unfortunate that the price will put the book out of the range of virtually all private individuals and most libraries. No doubt it will occur to many (however reprehensible the thought may be) that it could be Xeroxed for private study for less than one quarter of the published price always provided that a sufficiently affluent library could be located to borrow it from. N. N. GREENWOOD

Glacial Ages

The Late Cenozoic Glacial Ages. Edited by Karl K. Turekian. Pp. xii+606. (Yale University: New Haven and London, August 1971.) $20; £9.

THIS book is a collection of essays by leading authorities on diverse aspects of Cainozoic glacial ages, presented at an international colloquium held in 1969 to honour the retirement of R. F. Flint. The editor of the book, K. K. Turekian, points out that glacial ages are now known to have occurred before the classical glacial Pleistocene, and that it is therefore necessary to consider the phenomena associated with glaciation as properties of the Late Cainozoic. Much of the new evidence concerning environmental history in the Late Cainozoic comes from studies of ocean sediments and many of the twenty-one essays in the book concern this aspect of the subject. The essays thus supply a geophysical and marine geological background against which we may view the more classical aspects of the Quaternary ice ages.

There have been huge advances in our knowledge of Late Cainozoic environments, both marine and continental, in the past ten years; for example, the knowledge of climatic history provided by oxygen isotopes in marine faunas and in Arctic and Antarctic ice, and the knowledge of vegetational history provided principally by pollen analysis. The value of this book lies in the synthetic accounts written by those who have been responsible for much of the important research of the past two decades. It is not possible to make a detailed inventory of the contents. The essays concern the Late Cainozoic history of the oceans (including plate tectonics), and of Antarctica, the climatic records found in ice cores (a very important recent development), carbon-14 variations in the atmosphere, eustasy and isostasy, glaciation and vegetational history in North America, the floral record of the European Late Cainozoic, faunal history in Europe and Asia and hominoid evolution in East Africa.

The book thus provides an extremely valuable and timely synthesis of the present state of the many aspects and methods of study of environmental history in the Late Cainozoic. All the fields of research represented are advancing rapidly and workers in Quaternary research will be indebted to the organizers of this colloquium for providing them with a stimulating survey of recent achievements and prospects in the elucidation of Late Cainozoic Earth history. R. G. WEST

Gas/Metal Interface

Chemisorption and Reactions on Metallic Films. Edited by J. A. Anderson. Vol. 1: Pp. xii+555; £11; $32. Vol. 2: Pp. xii+323; £7; $21. (Academic: London and New York, August 1971.)

THESE two volumes comprise nearly 900 pages and cost £18 for a text that is well produced, except that almost every international convention regarding abbreviations, units and the printing of physical quantities in italic (or sloping) type, has been disregarded, and none of the authors has used SI units.

A book of this title fulfils a need and its appearance is timely. Its purpose is to describe with some degree of coherence and continuity the contributions to our understanding of the chemistry of the metal/gas interface in relation to the structure of metal films. The objective has only been partly achieved, because many of the authors have written about the topic of the chapter heading and have forgotten the principal title of the book. There is, in consequence, much valuable information about the formation and structure of films, and also about the chemisorption of gases on metal surfaces, but little correlation between these two groups. Each author has apparently been largely unaware of the contents of the other chapters, so that there is a fair measure of overlap and no overall coherence.

Scientists should first judge the relevance of the material about which they write and secondly express themselves concisely. There is little advantage to the reader in being presented with a series of review articles containing a large amount of descriptive detail both about the results and the workers who obtained them. Some judgment and critical assessment, even if biased, of the present status of the art are surely preferable.

In this respect, D. F. Klemperer's article is scholarly and critical; and he provides a well-organized account in admirably concise prose, yet the chapter is still extensively and well documented. The material is aptly chosen and is indeed directed to the use of metallic films as a primary consideration. J. V. Sanders in his chapter on structure of evaporated metal films has also the interests of experimental surface chemistry in mind by concentrating on structure in relation to the deposition parameters in film preparation and he provides guide-lines for the control, at least in part, of porosity, grain size, the quality of epitaxial layers and so forth, while emphasizing that it is by no means clear what conditions of preparation will produce either facets of close-packed atoms, or randomly oriented surfaces with kink and ledge atoms; and their surface properties may be quite different.

In contrast, the two long chapters by J. W. Geuss on fundamental concepts in film formation and on the influence of adsorption on electrical and magnetic properties are expansive reviews, written in verbose style. Judged in isolation, these chapters contain much good material and have considerable merit; in terms of the chief theme of the book, one must question the relevance of much of its contents. It requires ingenuity to transpose information about migration of metal atoms over a field emission tip, or the thermal accommodation of such atoms on the cleavage plane of an ionic crystal, to the problem of chemisorption of a gas on metallic films. Many people have doubts about the assessment of conductivity results on films and of their theoretical interpretation in terms of adsorbate–adsorbent bonding, so that in terms of the price of the present volume, a much shorter chapter could have been more appropriate.

D. O. Hayward in his chapter on gas adsorption clearly has an important task to perform. Except for some short sections on heats of chemisorption and desorption spectra of gases from metallic films, he has largely confined attention to an undefined metallic plane or to specific planes of metal crystals. He panders to convention by a necessarily superficial account of band theory, and then reverts to localized band concepts and surface geometry as an explanation of different adsorption states. The recent literature is well reported but the reader is given little help in understanding the significance of the wealth of detail presented. With greater selectivity and better organization, and a more concise style, an even more valuable contribution would have resulted.

In the final chapter in the first volume on infrared spectra of surface species, J. H. Little provides an abbreviated version of his 1966 book. The contributions of Greenler, both theoretical and experiment, on the multiple reflectance technique, and the interferometric studies of Low, are, however, included. Nevertheless, the impression gained is that one should concentrate on oxide surfaces in order to exploit more fully this technique.

J. Anderson (the editor) and B. G. Baker contribute the first two chapters in the second volume on adsorption, kinetics and surface structure and catalytic reaction on metal films. In the first chapter, a concise relevant account of structure, porosity, sintering and heterogeneity of films is followed by a good outline of equilibrium adsorption and rates of adsorption on a uniform surface as an introduction to an extension to heterogeneous surfaces. It has not been possible to treat reaction with films in an explicit manner, but at least the problem has been posed and recognized.

It is extremely difficult to write about catalytic reactions; the experimental data are varied and irreproducible, and to provide any general coherent theoretical account is not really possible. The reactions chosen are: exchange, hydrogenation, hydrogenolysis and skeletal somerization, and oxidation and dehydrogenation. They are treated at a phenomenological level in an attempt to give a general understanding of the nature of catalytic reactions on metal surfaces and a guide to the vast literature on this subject; in this sense, the contribution is a valuable and successful one.

The final two chapters deal with the properties and reactions of alloy films by D. R. Rossington, and oxidation of evaporated films by I. M. Ritchie. The first of these is a very good article and is directed throughout to films. The preparation, characterization and structure of films, with particular reference to the composition of the surface, are reported competently before the sections on the surface properties and the catalytic activity in parahydrogen conversion, oxidation reaction and ethylene hydrogenation. The material has been well organized, selected with judgment, and presented with clarity.

Ritchie has written an interesting and critical chapter—it has a freshness, largely because of its selectivity and critical approach. Oxidation of metals precedes that of films; the limited information derived from purely kinetic relationships is emphasized and other approaches are examined. The concepts are then discussed in relation to films and the further restrictions on the interpretation of results by the film structure qualitatively examined in a workmanlike manner.

In conclusion, although the chief purpose of the book has only been partly attained, surface chemists interested in the gas/metal interface and in metallic films should use all their persuasive powers to ensure that a copy of this book is available in an accessible library. F. C. TOMPKINS

CORRESPONDENCE

Publication Speed

Sir,—Your recent editorial (*Nature*, **233**, 294 ; 1971) on multiple publication seems to me to put the responsibility of the journals for this practice at a lower value than the facts would merit. You merely suggest that the slowness of the whole process of publication has some effect on the willingness of scientists to "leak" to newspapers before publication. It is, however, quite clear that the frequent lack of efficiency in the processing of articles submitted to learned and technical journals could function as a strong incentive to submission of papers to several journals simultaneously. Old news is no news, in science as elsewhere, and scientists are concerned to have their material appear in print as quickly as possible. If journals appear to reject papers arbitrarily then there is, from the author's viewpoint, something to be gained from a course of action which avoids the possibility of being left six months or even a year behind the field with a perfectly good but homeless paper.

The experience of some members of this laboratory would certainly indicate the need for a certain amount of reform in the way journals are run. I myself am co-author of a paper submitted to a reputable journal in February 1970 which was at first rejected and then, having been refereed again, was accepted in a revised form. This took the remainder of the year although the actual rewriting took perhaps three weeks. This paper has still not appeared, after nearly two years. A second paper for the same journal has been refereed (this took seven months) and has just been rejected by an editorial fiat that the subject matter is not relevant to the journal's interest although the scientific merit is unquestioned. Why could this decision, if justified, not have been made by the editor when he received it? The nature of the subject matter was clear from the title and abstract. An article submitted for the features pages of the journal of an engineering institution was with the editor for three months, at the end of which time he had it set up in type, before he acknowledged receipt of the article. At this point he decided that it was more suitable for the proceedings and scientific papers section of the journal and submitted it to the papers committee of the institution. Another decision which would have been better made at the earliest opportunity.

If editors are willing to countenance in themselves such a lack of regard for the interests of contributors, then they must take the consequences, which may well include multiple publications. Authors should not be expected to sit helpless before this sort of treatment which, in many cases, decreases the value of their work. Editors should acknowledge receipt of papers, reply to authors' letters in less than the month which is common, should as a matter of course prompt referees into faster reading and should make their editorial as distinct from their scientific decisions at an early rather than a late date. They may then find themselves better served by contributors.

Yours faithfully,

I. D. Griffiths

The Electricity Council
Research Centre,
Capenhurst,
Chester

Forecasting

Sir,—In your editorial "How Much is Enough?" (*Nature*, **234**, 115 ; 1971) you discuss the difficulty of forecasting population growth, and you ask whether the forecaster—in this case the Government Actuary—should "settle for more modest but more realistic goals". An interesting question, but not confined to the prediction of population.

In any organization concerned with products—schools, hospitals, food supplies, aircraft, weapons—of long gestation, there is always a wish to know the future so that policies can be tailored accurately to meet world conditions as they will exist ten or more years hence. And so there is pressure to forecast not only populations but also social and political attitudes, economic conditions, technological developments and so on.

When these questions are posed, they are answered: "forecasting" has achieved a respectability undreamt of by the seers of the Middle Ages. The forecasts provided become, too often, the single set of assumptions on which planning is based. If the forecast should prove accurate, then the policy-makers are labelled "far sighted"; if not, they are, with hindsight, abused for having backed the wrong horse. But might it not be wiser to accept that forecasting is not an exact science. We have the evidence of grossly misleading population predictions; we know that political attitudes can change markedly within a few months; social attitudes appear essentially unpredictable in the longer term; technological forecasts merely reflect an obvious truth that the more money and effort is poured into any project the faster it will move. Against this sort of background, might it not be that the sensible approach is to seek to build a system reasonably matched to a wide range of possible futures rather than closely matched to a single predicted future?

Yours faithfully,

I. J. Shaw

"Woodilee",
Mellersh Hill Road,
Wonersh Park,
Guildford, Surrey

Protecting Potatoes

Sir,—Under the headline "A Sticky End" (*Nature*, **233**, 93; 1971) your correspondent gave recognition to an interesting piece of work by Dr R. W. Gibson on the part played by glandular hairs in providing resistance to aphids in three species of potatoes (*Ann. Appl. Biol.*, **68**, 113; 1971). Gibson showed that glandular hairs on the potato species *Solanum berthaultii*, *S. tarijense*, and *S. polyadenium* discharged a gummy exudate which eventually immobilized the aphid and led to its death through starvation. As noted by Gibson this type of mechanism has potential value in the control of aphid population build-up. This effect may be further enhanced if combined with other types of resistance to aphids, such as the resistance to feeding demonstrated in several potato species, including *S. polyadenium*, by J. B. Adams at this research station. Control of aphid populations in such ways as these has the additional effect that it reduces the rate of spread of certain aphid-borne viruses.

The key to the utilization of these

traits lies in the practicality of incorporating them into the parental lines used in potato breeding programmes. Gibson recognized this, and noted that *S. tarijense* may be crossed with the cultivated potato. Your correspondent, however, gives the impression that the problems in utilizing these species are completely unknown. This is far from the case.

S. berthaultii and *S. tarijense* are diploid species and both can be crossed easily with the cultivated potato, the tetraploid *S. tuberosum*. The progeny from such crosses are sterile triploids which would still carry many undesirable traits from the wild species. However, both these species can also be crossed with haploids (dihaploids) of *S. tuberosum*, and with haploid derivatives, to give progeny which are diploid and, when the wild species is used as the seed parent, are also generally fertile. Undesirable traits may be eliminated by further crossing and selection. *S. polyadenium*, on the other hand, can at best only be crossed with *S. tuberosum* with very great difficulty.

It is clear that of the species studied by Gibson two, *S. berthaultii* and *S. tarijense*, can be used in a breeding programme fairly readily. Working at the diploid level, as I have suggested, has numerous advantages, and there are several methods of combining diploid parental lines and tetraploid cultivars at the final stage before variety selection.

Yours faithfully,

T. RICHARD TARN

Canada Department of Agriculture,
Research Station,
Fredericton, New Brunswick

Unambiguous Billion

SIR,—For a long time we have had to live with the annoying fact that Americans and Europeans cannot use the word billion without a risk of confusion. Perhaps it would be possible to persuade people on both sides of the Atlantic to add just two extra letters to indicate how big the billion is meant to be. To be specific, I suggest that 1 ambillion$=10^9$ and 1 eubillion$=10^{12}$. Thus ambillion becomes the name of the American billion—a cause of ambiguity.

Yours faithfully,

J. HILDEN

Department of Statistics,
University Institute of Medical Genetics,
Copenhagen

Retino-rectal Connexions

SIR,—Dr Robertson (*Nature*, **233**, 435; 1971) refers to an annoying visual condition which he calls tunnel vision. Surely he means hindsight?

Yours faithfully,

F. H. ALLEN
N. W. ISAACS

University Chemical Laboratory,
Lensfield Road,
Cambridge CB2 1EW

Obituary

Professor Arne Tiselius

PROFESSOR ARNE TISELIUS, who won the Nobel Prize for chemistry in 1948, died in Stockholm on October 29, aged sixty-nine.

Born in Stockholm in 1902, Tiselius moved early to Gothenburg and thence, after matriculation, to take up academic studies in Uppsala, the city which he was rarely to leave. Tiselius's interest in chemistry was first awakened at school, and his ability was noticed by The Svedberg, who quickly made him his valued and trusted research assistant. The master soon gave his protégé the freedom to plan and carry out his research. Tiselius chose to investigate electrophoresis and studied in particular the so-called boundary anomalies which occur in connexion with the electrophoretic migration of proteins. In his doctoral dissertation in 1930, Tiselius presented significant discoveries on the heterogeneity of serum proteins. After an important year of research at Princeton, he continued his development of moving boundary electrophoresis and designed the apparatus which made his name internationally known, the chief improvement being the elimination of convection. Tiselius showed by means of this apparatus that the electrophoresis of serum gave five distinctly migrating boundaries. These are albumin, and α, β and γ globulin as Tiselius designated them, and also a boundary dependent on the protein concentration. This work brought the world's leading immunochemists to Uppsala and the international contacts in many fields of physical chemistry and biochemistry were intensified. In 1938 Tiselius became the first to hold a newly created research chair in biochemistry at Uppsala.

Tiselius took an active part in the development of electrophoresis and especially preparative zone electrophoresis, but he extended his interest to chromatography which he realized was to provide biochemists with the necessary methods for further investigating the chemistry of proteins. He introduced a standard nomenclature for chromatography and contributed especially to the development of general principles for analytical and preparative chromatography.

For example, displacement chromatography and gradient chromatography originate from Tiselius's pioneer work. Gas chromatography can also be traced from the Uppsala school. These methods have extended far beyond the field of protein chemistry. Tiselius's last work as an active researcher was to investigate suitable conditions for the chromatography of proteins. His contribution was the introduction of calcium phosphate as an adsorbent, which method is still being used. When ion-exchangers and molecular-sieving gels were introduced he retired from experimental work but followed developments with never ending interest and gave generously of his knowledge to others.

After receiving the Nobel Prize in 1948 Arne Tiselius increasingly began to devote himself to research policy. He was President of the International Union of Chemistry IUPAC from 1951–1955.

Swedish science is greatly indebted to Arne Tiselius. He was, for example, one of the initiators for the founding of the Swedish Natural Science Research Council.

He became the presiding chairman of the Royal Academy of Science in 1956 and was very active in the Nobel Foundation, and held, among other posts, the chair between 1960–64. He took a keen interest in the Foundation's symposium committee and took the initiative for several of the international symposia. He was also a member of the Wallenberg Foundation.

Tiselius's contributions to the international coordination of research in chemistry have been of utmost importance and the appreciation resulted in eleven honorary degrees. He belonged to a great number of academies and learned bodies and was on the editorial committees of a number of scientific journals. His capacity for work was almost unbelievable and he was always in great demand.

Tiselius was deeply and personally involved in the problems arising from the effects of scientific research on society and man, and he expressed his anxieties for the negative effects in the Pugwash movement.

Arne Tiselius was not only a brilliant scientist, but also an unusual personality. He possessed a rare ability for listening to others' opinions, drawing conclusions, seeing the essentials, summarizing and then presenting the judgment and advice of a good friend and wise leader. He will be sorely missed.

Announcements

International Meetings

December 28–31, **Association for Science Education Meeting,** Stirling (Mr J. Keri Davies, Education Department, University of Stirling, Scotland).

January 4, 1972, **Plant Constituents of Pharmacological Interest,** London (Mr R. E. M. Marshall, Pharmaceutical Society, 17 Bloomsbury Square, London WC1).

January 4–7, 1972, **Society for Experimental Biology Conference,** London (Mr T. M. Preston, Department of Zoology, University College, Gower Street, London WC1).

January 5–7, 1972, **Increasing the Biological Contribution to the Control of Pests and Diseases,** Oxford (Society of Chemical Industry, 14 Belgrave Square, London SW1).

January 6–7, 1972, **Biology of the Cell Membrane,** Amsterdam (Dr J. James, Histological Laboratory, Jan Swammerdam Institute, 1st Constantijn Huygensstraat 20, Amsterdam, Holland).

January 7, 1972, **Sampling of Mineralogical and Geological Materials,** London (The Secretary, The Institute of Mining and Metallurgy, 44 Portland Place, London W1N 4BR).

January 10–12, 1972, **Surface Physics of Semiconductors,** Southampton (Dr D. R. Lamb, Department of Electronics, University of Southampton, Southampton SO9 5NH).

January 11, 1972, **Unconventional Nitrogenous Sources for Feeds and Foods,** London (Mr N. R. Jones, BFMIRA, Randalls Road, Leatherhead, Surrey).

January 18, 1972, **The Prevention of Air Pollution from Incineration,** Manchester (The Filtration Society, 1 Katharine Street, Croydon CR9 1LB).

January 25, 1972, **Lipoprotein Phenotyping,** London (Dr B. Lewis, Department of Chemical Pathology, Royal Postgraduate Medical School, Ducane Road, London W12 0HS.

February 21–25, 1972, **Photo Interpretation for Industry and the Environment,** London (N. Lindsey, The City University, St John Street, London EC1V 4PB).

February 23, 1972, **Anaesthetic and Neuromuscular Blocking Drugs,** London (Dr A. B. Simmonds, Chelsea College, Manresa Road, London SW3).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Royal Observatory Bulletins. No. 162: Optical Positions of Radio Sources. By C. A. Murray, R. H. Tucker and E. D. Clements. Pp. 215–238. 50p net. No. 164: The Isaac Newton Telescope Cassegrain Spectrograph. By G. A. Harding and M. P. Candy. Pp. 251–256. 20p net. No. 166: The Statistics of the Nearby Stars. By Sir Richard Woolley, Susan B. Pocock, Elizabeth A. Epps and Rosalind Flinn. Pp. 275–299. 40p net. (Herstmonceux: Royal Greenwich Observatory, 1971.) [238

Forestry Commission. Library Catalogue of Books. Pp. 176. Horticultural Uses for Bark. Pp. 8. Research and Development Paper No. 81: Forest Management for Conservation, Landscaping, Access and Sport. Pp. 30. (London: Forestry Commission, 1971.) [248

Philosophical Transactions of the Royal Society of London. B: Biological Sciences. Vol. 262, No. 842 (20 August 1971): A Discussion on Active Transport of Salts and Water in Living Tissues. Organized by R. D. Keynes, FRS. Pp. 83–342 + plates 23–35. (London: The Royal Society, 1971.) £7.80; $20.30. [248

Shipbuilding and Shiprepairing. Pp. 10. (London: Commission on Industrial Relations, 1971.) [268

Trada 70—Report of the Director of the Timber Research and Development Association. Pp. 12. (London: Timber Research and Development Association, 1971.) [268

Political and Economic Planning. Broadsheet 530: Work Camps and Volunteers—The PEP Study of International Work Camps in Britain and British Work-Camp Volunteers. By Michael Thomas. Pp. iii + 93. (London: PEP, 1971.) £1. [278

Science Research Council. Royal Observatory, Edinburgh. Publications—Vol. 7, No. 5: Photographic V and R Magnitudes of T Tauri Stars and Related Objects in Orion. By M. T. Brück. Pp. 63–72. (Edinburgh: The Royal Observatory, 1971.) [278

Philosophical Transactions of the Royal Society of London. B: Biological Sciences. Vol. 262, No. 843: Ontogenesis of Corneal Surface Ultrastructure in Nocturnal Lepidoptera. By G. Gemme. Pp. 343–363 + plates 36–53. £2; $5.20. Vol. 262, No. 844: Synaptic Organization of Cone Cells in the Turtle Retina. By A. Lasansky. Pp. 365–381 + plates 1–8. £1.70; $4.40. (London: The Royal Society, 1971.) [278

The Zoological Record, 1969, Vol. 106, Section 8: Bryozoa (Polyzoa) and Entoprocta. Compiled by the Staff of the Zoological Society of London. Pp. iv + 16. (London: The Zoological Society of London, 1971.) £3.50. [318

Environmental Studies: The Construction of an 'A' Level Syllabus. Compiled by S. McB. Carson. Pp. 158. (London: National Foundation for Educational Research in England and Wales, 1971.) £1 (by post £1.10). [318

British Medical Bulletin, Vol. 27, No. 3 (September 1971): Symposium on "Cognitive Psychology". Pp. 191–290. (London: The British Council, 1971.) £2. [318

The Hannah Dairy Research Institute. Report for the Three Years ended 31st March, 1971. Pp. 78. (Ayr: The Hannah Dairy Research Institute, 1971.) [19

Calendar of the Countryside for 1972. (London: Christian Action Publications Limited, 1971.) 75p (postage 5p). [19

The Scottish Horticultural Research Institute. 17th Annual Report for the year 1970. Pp. 69. (Invergowrie, Dundee: The Scottish Horticultural Research Institute, 1971.) [29

Department of Trade and Industry: Safety in Mines Research Establishment. Safety Research. Pp. 32. (Sheffield: Safety in Mines Research Establishment, 1971.) [29

Swansea Tribology Centre. Annual Report 1969–1970. Pp. 15. (Swansea: Swansea Tribology Centre, University College of Swansea, 1971.) [39

Writing a Scientific Paper. By Vernon Booth. Pp. 21. The Design of Laboratories for Radioactive and Other Toxic Substances. By Dr D. Hughes and R. Cullingworth. Pp. 32. (Colnbrook, Bucks.: Koch-Light Laboratories, Ltd., 1971.) [69

Annual Report of the Soil Survey of England and Wales 1970. Pp. 35. (Harpenden, Herts.: Soil Survey of England and Wales, Rothamsted Experimental Station, 1971.) [69

Phosphate Fertilizer Sources: Agronomic Effectiveness in Relation to Chemical and Physical Properties. By Dr G. L. Terman. Pp. 29. (London: The Fertiliser Society, 1971.) [89

Royal Observatory Bulletins, No. 153: Magnetic Results 1962, 1963 and 1964 (Hartland). Pp. 175–346. (London: HMSO, 1971.) £1.50 net. [89

Building Research Station Digest, No. 133: Concrete Pumping. Pp. 4. (London: HMSO, 1971.) 5p. [109

Other Countries

State of California. The Resources Agency, Department of Fish and Game. Fish Bulletin 151: Migrations of Adult King Salmon *Oncorhynchus tshawytscha* in the San Joaquin Delta as Demonstrated by the Use of Sonic Tags. By Richard J. Halloch, Robert F. Elwell and Donald H. Fry, Jr. Pp. 92. Fish Bulletin 153: The California Marine Fish Catch for 1969. By Leo Pinkas. Pp. 47. (Sacramento, California: Department of Fish and Game, 1970.) [138

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Debate without Raised Voices

HOWEVER unsatisfactory may be the outcome of the discussion of the future of British science policy provoked by the publication of the government's green paper containing the Rothschild and Dainton reports (see *Nature*, **234**, 169; 1971) there is very little doubt that the occasion will provide yet another demonstration of the gentility of British public life. So far, the people most affected have been muttering to themselves and to their friends about the iniquities of one or other (and sometimes both) of the two documents, but there has been no sign so far of the kind of intellectual debate which the issue deserves. Christmas, perhaps, may be a diversion, although there is every reason to hope that the scientific community will not put turkey and plum pudding before its more lasting interests. It is also to be hoped that when eventually people start responding to the government's plea that interested parties should have their say, they will do so in language free from the ritual cant with which the subject is usually blessed. Last week, Dr G. J. Leigh began a statement on the subject with the words "The Rothschild report and recommendations present a threat to the well-being of British science which must be resisted". And the annual meeting of the Medical Research Society on December 10 adopted a formal resolution that "this society disagrees entirely with the principles stated in the report by Lord Rothschild . . .".

The weakness in these formal statements of opposition to the Rothschild doctrine that research policy should be determined by the demands made by customers (government departments) on research councils and their establishments is that they imply that the conduct of scientific research is an autonomous process in which the balance of effort is not determined by the wish somehow to obtain practical benefits. In practice, however, the research councils most directly threatened by the Rothschild proposal—the Natural Environment Research Council, the Agricultural Research Council and the Medical Research Council—have all relied in recent years on the argument that their activities are of practical value. Moreover, nobody will dispute that immense benefits have been won from much of the work that has been carried out under the umbrella of the research councils—the strains of wheat which the Agricultural Research Council have developed have been, for example, a great practical and economic benefit. In other words, although there may be some who object as the Medical Research Society apparently does to the principle of the Rothschild report, most students of the question will agree that the overriding issue is not whether customers of one kind or another should make demands on the research councils but that of knowing how best these demands might be made. On this point, Dainton and Rothschild share common ground, for the Dainton report says that in the years ahead, "research councils will have to become increasingly well informed about national needs and objectives so that they may try to deploy scarce resources in the most appropriate directions and be seen to be doing so". In other words, the Dainton view is that the research councils should comprise enough skill and understanding of practical problems for them to be able to make coherent demands on laboratory scientists. What this implies is that the two reports differ only in the arrangements which they suggest for expressing the interests of the ultimate beneficiaries, the British taxpayers, in language that can be used to define a programme of research.

What kinds of questions should be asked of the research councils? Implicit in Sir Frederick Dainton's definition of strategic research, that kind of scientific activity considered likely to lead to beneficial results which is nevertheless unpredictable in character, is that there are limits inherent in the character of the scientific process to the precision with which goals can be defined in advance. So far as the Dainton report is concerned, it would be entirely proper for government money to be spent under the banner of strategic research on a comprehensive investigation of the physiology of domestic farm animals because of the near-certainty that in the decades ahead, a better understanding of animal physiology will be of great practical importance in agriculture.

As things have turned out, this is precisely the point of view which Lord Rothschild rejects. To him, such an investigation is far too unspecific. To him, the questions to ask are questions such as "Is it feasible to think of developing Christmas turkeys weighing substantially more than those at present on the market and, if so, what kind of a research programme would be necessary and how much would it cost?" This is exactly like the question whether it is feasible to think of developing a supersonic aircraft and, if so, what kind of a research programme would be needed and how much would it be likely to cost? The real issue between Rothschild and Dainton is not whether questions like these are valuable questions—and some, of course, say that they are indecent—but how extensive is the field of enquiry in which they can be useful guides to the development of research policy. This, as it happens, is an empirical question, not an issue of principle. Those who pretend otherwise are turning the debate on research policy (such as it is) into the intellectual equivalent of a mediaeval joust, with Rothschild and Dainton as tin-clad champions.

Another Notch in the Tightening Belt

THE publication of the British government's forecast of public expenditure between now and April 1976 which appeared a month ago (*Public Expenditure to 1975–76*, Cmnd. 4829, HMSO, £0.68) is a solemn warning that, however the dispute between Dainton and Rothschild may be resolved, there are hard times ahead for scientific research and development. The object of publishing estimates of public expenditure well in advance is quite properly to provide a framework within which later political decisions about the direction of government policy may be determined, and it is only fair to say that this year the Treasury has done better than ever. It may be a long time before forecasting of public expenditure is done with as much detail as it might be, with the costs of alternative programmes shown separately, but the British government has at least gone a long way in spirit to meet the recommendations of the Select Committee on Government Expenditure a year ago. But even if there are plenty of opportunities for changing government policy on such things as money for the research councils or for various government establishments, the estimates of forward expenditure which have now been provided offer very little hope of a change in the scale of finance for research and development in Britain in the next two or three years. If anything, and if present tendencies continue, even less money will be spent in 1975 than in the present year.

In the current financial year, for example, the research councils are likely to cost £125 million—the Science Research Council will consume £56 million or roughly 45 per cent of all government expenditure on basic civil research. The forward estimates now published suggest that this sum will increase to £134 million in 1973–74 and £137 million in 1974–75. These figures entail reductions from previous estimates—for policy reasons, for example, the government now says that the research councils will have £3 million less to spend in 1974–75 than had been intended a year ago. Why should this be? The government says that it has tried to bring the growth of expenditure "more into line with that of public expenditure programmes as a whole". At the beginning of the next five years, the rate of growth of the combined budgets of the research councils will be about four per cent a year, but by the end of the period, the Treasury congratulates itself, the rate of growth will be identical with that of public expenditure as a whole. The result, of course, is quite predictable. Five years from now, the research councils will not be able to provide research grants and studentships in larger numbers than at present even though, by then, the university system will have grown by something like 30 per cent. Moreover, the government has plainly set its face against the concept of what is called sophistication—the tendency for ever more expensive and intricate equipment to become available for carrying out specific jobs. Only two years ago, the Department of Education and Science was estimating that, on this account alone, it would require that an extra four or five per cent a year should be made available simply so as to keep the then scientific labour force at work on basic research fully employed.

If the research councils are in for a hard time, so too are the research and development organizations supported by the Department of Trade and Industry. The white paper now published reckons that the research establishments supported by the department will cost £61 million in the present financial year but merely £40 million four years from now, in 1975. The laboratories concerned include those of the Atomic Energy Authority as well as national institutions such as the National Physical Laboratory, the National Engineering Laboratory and the Warren Spring Laboratory. The white paper says that much of the saving of £20 million expected in the next five years will come about because the Atomic Energy Authority will be concentrating increasingly on fast reactors for the nuclear power programme, but it also says that the industrial research establishments and the Atomic Energy Authority are continually trying to recruit commercial work from outside the government. The implication is that the cost of nuclear energy research as such will decrease by about £10 million and that, if there is to be no physical contraction of the research establishments, the laboratories between them will have to raise something like £10 million a year in commercial contracts. The Atomic Energy Research Establishment at Harwell has been doing splendidly in the past few years, but it remains almost the only laboratory of its kind to have made substantial business as a commercial research undertaking. Even the most optimistic supporter of the doctrine of commercial business in government laboratories will be hard pressed to see how other establishments could grow as quickly in this direction as the white paper implies. It follows that the government must have at the back of its mind an actual decrease in the size of some of the establishments. The question it seems not to have asked itself is whether the time may not be coming when one of the most effective ways of spending public money is to devise ways of channelling funds towards industrial enterprises which are likely to be commercially successful in a comparatively short time. If Britain is ever to carry out the development of a reasonably successful typewriter or sewing machine, or one of the other products of profitable technology, the chances are that the government itself will have to take a lead.

To protest that changes like these, spread as they are over the next five years, represent an attack on scientific research and development would of course be foolish. Quite possibly, the government is calculating that decreases in public expenditure will be more than compensated for by increases in the amount of money spent by industrial companies but the statement last month is entirely silent on that subject. Moreover, it is clear that the government intends to reduce as far as possible such things as its support for industrial projects of other kinds—both the National Research Development Corporation and the computer companies which have benefited from government support in the past few years are in for leaner times. The difficulty in all this is of course that nobody has ever thought out the scale on which the British government should support scientific research and development both through the research councils and in industry. In spite of all the fuss now under way about the Rothschild proposals, these are strictly concerned with organization. Nothing is said about the scale on which expenditure would be desirable and, for that matter, nothing is said about the framework within which public support for industrial research as distinct from the kind of research which the research councils carry out should be undertaken. But these are small parts of the government's interest in research and development.

Last year, defence research accounted for 40 per cent of all government expenditure on research and development and although the proportion has been falling steadily for several years, it is hard to think it wise for expenditure on such a scale to continue much longer without a thorough investigation of the principles on which the money should be allocated to different causes. The result of all this, of course, is the paradox that while the scientific community in Britain has its interest chiefly engaged in an important but essentially organizational question about the best way of allocating funds to one part of publicly supported civil research, the government is perpetrating policy decisions about the scale of its involvement in research and development as a whole in the years ahead which have serious consequences for the scientific community and which may even be unwise as well.

Fishing in European Waters

FISHERMEN are understandably among the most vociferous and conservative members of any community, which is no doubt why it has taken such a time for the government now seeking membership of the European Communities to reach an understanding on fishing policy. On December 12, the representatives of Britain, Ireland and Denmark seem to have reached an accommodation with Brussels on a fishing policy for the next decade, but the government of Norway will come back next year to resume negotiations which are plainly turning out to be so complicated that Norway may yet finish up outside the European Communities. For the remaining countries, the new agreement on fisheries is in fact more than generous.

Unhappily, there is nothing in this agreement to ensure that the decade ahead will be one in which fish in north-west Europe are free from the pressures of over-fishing which are at present a far greater danger to their survival than any other influence. In the years since the Second World War, herring have been seriously damaged by over-fishing, which is why it is encouraging that the North-East Atlantic Fisheries Commission apparently agreed at its meeting in Moscow last week to impose not merely a closed season on herring fishermen but also restrictions on the permissible catch as well. Only time will tell if these new proposals will be less toothless than the regulations with which the International Whaling Commission has failed to protect blue whales in the South Atlantic, but there is always room for hope.

The long haggle in Brussels over the precise regions of the European coast to be fished by vessels of different nationalities has more acutely drawn attention to the folly of attempts to conserve the stocks of fish in the waters off north-west Europe by the arbitrary methods now sought. A part of the trouble, of course, is that even the agreed twelve mile limit does not necessarily contain all the breeding grounds where most damage might be done by over-fishing. If it is intended that there should be a European fisheries policy, it should at least cover the whole of the North Sea and those parts of the Western Approaches which are accessible to rational study. The second difficulty which has emerged in the past few months is that very little is known of the biology underlying the productivity of the European fisheries. Is it possible, for example, that the remarkable increase in the numbers of young haddock and whiting in the North Sea within the past decade is to be linked with the way in which the herring have declined in the same period? The species do not compete for a common food supply but there may be other influences at work. And why is it that the Plymouth herring has chosen this time to return in strength? Is there some secular change of climate? Is it possible that pollution, on the moderate scale on which organic nutrients find their way into the North Sea and similar basins, is actually a help and not a hindrance? These are all questions which need to be much more adequately understood before a permanent fisheries policy is negotiated, and for this reason it is entirely welcome that Mr Geoffrey Rippon should have told the House of Commons last week that he had urged on the European Communities "the need for common action in all our interests to ensure conservation of stocks". Unhappily, so far as can be told from government departments, Mr Rippon has no specific proposals for setting up machinery to regulate fisheries on a European basis. It is to be hoped that he and his colleagues will not wait for the whole decade before clearing their minds.

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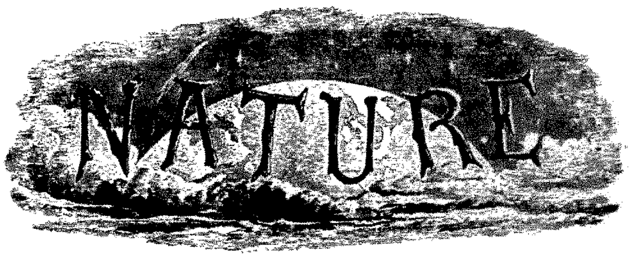
100 Years Ago



MANCHESTER

Literary and Philosophical Society, November 28.—Dr. J. P. Joule, F.R.S., vice-president, in the chair. "Encke's Comet and the Supposed Resisting Medium," by Professor W. Stanley Jevons. The observed regular diminution of period of Encke's comet is still, I believe, an unexplained phenomenon for which it is necessary to invent a special hypothesis, a *Deus ex machina*, in the shape of an imaginary resisting medium. I cannot be sure that the suggestion I am about to make has not already been made, but I have never happened to meet with it; and therefore I venture to point out how it seems likely that the retardation of the comet may be reconciled with known physical laws. It is asserted by Mr. R. A. Proctor, Prof. Osborne Reynolds, and possibly others, that comets owe many of their peculiar phenomena to electric action. I need not enter upon any conjectures as to the exact nature of the electric disturbance, and I do not adopt any one theory of cometary constitution more than another. I merely point out that if the approach of a comet to the sun causes the development of electricity arising from the comet's motion, a certain resistance is at once accounted for. Wherever there is an electric current, some heat will be produced and sooner or later radiated into space, so that the comet in each revolution will lose a small portion of its total energy. In the experiments of Arago, Joule, and Foucault, the conversion of mechanical energy into heat by the motion of a metallic body in the neighbourhood of a magnet was made perfectly manifest. If then there is any magnetic relation whatever between the sun and the comet, the latter will certainly experience resistance. The question is thus resolved into one concerning the probability that a comet would experience electric disturbance in approaching the sun. On this point we have the evidence now existing that there is a close magnetic relation between the sun and planets. If, as is generally believed, the sun-spot periods depend on the motion of the planets, a small fraction of the planetary energy must be expended.

From Nature, **5**, 174, *December* 28, 1871

OLD WORLD

MUSEUMS

Money for Monuments

A GOVERNMENT grant of £200,000 a year to assist in the purchase of museum objects of industrial and technological interest is recommended by the Standing Commission on Museums and Galleries in a report published last week. It is recommended that the money should be spent in circumstances where at least 50 per cent of the cost of preserving the particular object can be obtained from other sources (*The Preservation of Technological Material*, HMSO, £0.365).

The money would be administered by an advisory committee to be set up by the Department of Education and Science and supported by a secretariat in the Science Museum, with an assistant keeper at its head, which would also offer assistance to other bodies on all aspects of the preservation of all types of technological material.

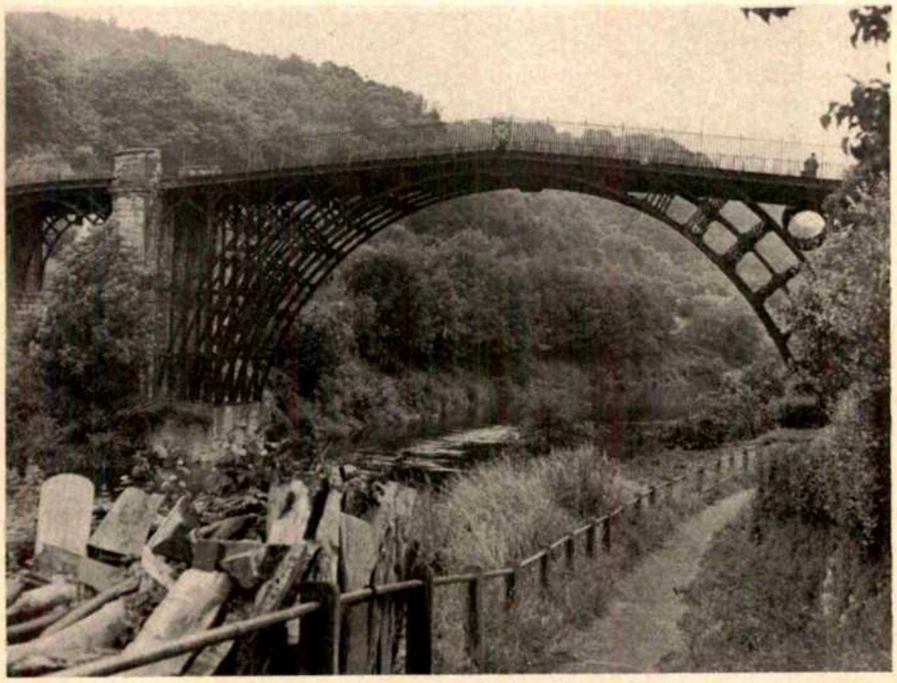
The working party says that the Department of the Environment, which has responsibility for *in situ* historical monuments in England, should spend more on their preservation while the Secretaries of State for Scotland and Wales should also endeavour to do the same for monuments in their respective countries.

The working party to investigate the problem of the preservation of technnological material was set up in 1970 by the previous government following a decade of mounting concern about the relics of technological developments in Britain. Several monuments have been lost in recent years—in several instances because there was not enough money available to purchase them in the limited time before they were to be destroyed. As typical examples the Sudbrook Engines that were used until 1967 by the Great Western Railway and then British Rail to pump the Severn Tunnel were at that time due to be scrapped. British Rail offered to preserve them *in situ* for a sum of £70,000 but as the money was not available they were destroyed.

At the moment there are some monuments that have been saved but which need a lot of money to restore them to their original condition. The SS Great Britain is now in a Bristol dry dock where she was built in 1843 and there are frenzied efforts in progress to raise money to restore the ship to her former glory. All the money so far has been obtained from a private benefactor and in spite of the interest shown by the iron and steel industry in preserving the ship there is still a need for more money.

There is an even more pressing need for financial contributions to save other relics of the Industrial Revolution. The Iron Bridge, in the village of that name in Shropshire, the first cast iron bridge in the world, is in need of funds to rectify the subsidence of two of its abutments. Unless money is available soon, it will not prove possible to preserve the section of the Menai Bridge that was badly damaged by fire in 1970. Temple Meads railway terminal, Bristol, designed by Brunel is the oldest remaining main line rail terminus in the world. It has three times in recent years been given a lease of life—the last time earlier this year when British Rail were refused permission to build an office block on the site of the terminus.

The secretariat to administer the £200,000 would be concerned with industrial monuments, relics of industrial social life, ships and relics of the shipbuilding and merchant shipping industries, art connected with industry and archives, including photographs and sound and film archives. The secretariat would consist of representatives of museums, Department of the Environment, as well as individuals who have knowledge of the history of technology. The working party recommends that the secretariat should have help when necessary from representatives of other bodies, such as the Public Record Office and the Royal Commission on Historical Manuscripts.



The Iron Bridge at Iron Bridge, Shropshire

SPACE

Britain Bows Out

BRITAIN'S request to withdraw from the European Launcher Development Organization (ELDO), made in Paris last week, means that Britain no longer has even a nominal interest in launcher development. The decision to withdraw is the logical result of the announcement in 1968 that Britain would not support an extension of the ELDO programme and would limit her financial commitment to £11 million from January 1, 1969.

The decision ties in with the scrapping of Black Arrow earlier this year (see *Nature*, **234**, 4; 1971) and underlines Britain's belief that the launcher needs of European space programmes can best be met by buying rockets from the United States. Britain is confident that American Scout rockets will be available whenever needed for her own satellite programme, and only last month the US State Department agreed in principle to provide launch facilities for the member countries of ELDO.

Other European nations, notably France and West Germany, are less happy to rely on the Americans for launchers and feel the development of a European rocket to be a necessity. The consistent failure of the Europa I launches, however, followed by the spectacular failure of Europa II last month does suggest that the development of a hybrid multinational rocket may not be a realistic possibility.

Britain's withdrawal, which due to ELDO's constitution will not become effective until January 1973, does not affect Hawker Siddeley Dynamic's contract with ELDO to supply Blue Streak, which forms the first stage of both Europa I and II.

Now that the United Kingdom is free of the shackles of a European rocket that does not work and a national one that was not sufficiently powerful, the £19 million spent on civil space in 1970–71 can be used for such things as satellite developments, both nationally and within Esro.

FOG CLEARANCE

No Clear Skies Yet

FOG is expensive. It costs time, money and lives. In just one nose to tail pile up in Britain last month, nine people died and fifty were injured. One day's fog at Christmas when planes are full could cost BEA alone £40,000, although money saved from cancelled flights would bring this figure down. Yet comparatively little research is done in Britain into fog dispersal.

Fog dispersal, whether of warm or cold fogs, is beset with a number of problems. Any dispersal process must operate continuously as mixing and drift within the fog rapidly fills in cleared spaces. Dispersal methods must not in themselves create equally serious hazards, and any method for frequent dispersal must be economically viable.

Supercool fogs are the easiest to disperse. Once the fog is below $-4°$ C silver iodide crystals, liquid propane or CO_2 can be dropped into it from aircraft, cooling the droplets so that they fall as snow. Alternatively, material can be forced into the fog by generators at ground level. Dispersal by these methods is used in Norway and North America and they are established techniques, the economics of which are viable if fogs are frequent.

Warm fogs, however, pose greater problems. During the war a system known as FIDO was used in Britain to improve visibility for returning bombers. This involved the burning of tons of oil along the runways. After the war it was abandoned in Britain on the grounds of cost and no commercial fog dispersal has since been attempted. FIDO was still used at Los Angeles airport until 1953, however, when cost and pollution put a stop to its use. It has been reconsidered in various forms from time to time—the latest suggestion being that North Sea gas should be used at Heathrow—but it is an extremely expensive system, causing severe turbulence around the runways, and flying through the ring of flame has been compared to going through hell. At Orly airport, near Paris, an Atar 101F jet engine has been installed on one runway, the heat of which evaporates fog. The system is considered semi-operational and to date no turbulence problems have been encountered, although only light aircraft have used the runways.

Successful dispersal has been achieved in America by flying a helicopter over the fog using the downdraft to blow the dry air above the fog down into it, thus drying the fog out. This method is also expensive, however, and only the Americans have helicopters capable of producing a large enough downdraft.

The approach that the Americans most favour, however, is seeding. Hygroscopic material is dropped into the fog to effectively dry it out. Common salt can be used, but the problems of corrosion that result from dropping tons of salt on runways may prove prohibitive. A number of American companies have taken out patents on chemical and detergent mixtures which, they claim, increase the cohesion of the droplets but the scientific basis for this has not been proved and in Britain it is doubted if these offer a real solution. The cost and effectiveness of both these approaches are questionable. Dr B. A. Silverman, of the USAF, estimated recently that to clear a fog over one runway, for one hour, to allow aircraft sufficient visibility to land would require the use of several large aircraft to seed-drop up to 100 tons of material at a cost of between $30,000 and $250,000 an hour. Dr Silverman predicted that in three to five years these systems will be in operation, but British researchers consider that a rather optimistic estimate.

Research in Britain concentrates on the fundamental microphysics of fog as it is felt that fog dispersal systems cannot be effectively assessed until fog is fully understood. In the United States research is concentrated on actual dispersal methods and considerable success is claimed for some of them. Earlier this month Northwest Environmental Technology was granted $159,000 by the Federal Aviation Administration to measure and evaluate seeding techniques, and Dow Chemical Company is part way through a $99,000 research programme.

For the immediate future, however, airlines prefer to put their money into blind landing systems as in reality economic warm fog dispersal is not just around the corner. The clearing of fog on motorways is completely out of the question for years to come, partly on the grounds of cost, and because of the impossibility of keeping the cleared patch where it is wanted.

EDUCATION

Teachers Taught

THE Royal Society's scheme to involve school teachers in academic research is now in its fourteenth successful year. The latest report of the society's Scientific Research in Schools Committee shows that 102 teachers are investigating diverse topics under the supervision of Fellows of the Royal Society and other eminent scientists. And as in previous years, several of the teachers have published their results in such auspicious organs as the *Journal of Animal Ecology* and *Spectrochimica Acta*.

When the committee was set up in 1957, thirty-three research projects were started in schools, with the pupils being encouraged to participate whenever possible, and by 1966 there were 107 projects in progress. One of the greatest benefits to the teachers is that this scheme can provide them with an enthusiastic and knowledgeable adviser who will often lend facilities and equipment as well as expertise. In this way some school teachers are able to continue work which they started while at university, and others can gain their first taste of research.

The committee is able to give financial help in the form of grants for equipment, sometimes as large as £600. As well as the Royal Society's own funds, the sources of this money include the United Kingdom Atomic Energy Authority, which has given up to £1,000 annually since 1963, and several large companies.

Last year grants totalled £2,250, but the decline from the £4,500 spent in 1969 is not a consequence of economic constraints; the projects on hand at the moment are just more modest in their requirements. They do not, however, seem to be any less ambitious. Topics under investigation in British schools include the application of gas chromatography to the study of reaction kinetics; the reproduction of the American cockroach; thermal degradation of phosphonitrilic isothiocyanate; erosion processes in the New Forest; and limiting factors in mice populations.

MACROBERT AWARD

Gas from Naphtha

THE MacRobert Award for 1971 has gone to a team of five researchers from the Gas Council for their work on gas manufacturing processes. The £25,000 award, which was instituted in 1969, goes to Dr F. J. Dent, formerly Director of the Gas Council's Midlands Research Station, and the team who worked with him—Dr Dennis Hebden, Mr George Percival, Dr Brian Thompson and Mr Ronald Edge.

The award is made for an outstanding innovative contribution in the fields of engineering, technology or the applied physical sciences which has enhanced or will enhance the prestige and prosperity of the United Kingdom. Previous winners are Freeman, Fox and Partners for their design of the Severn Bridge, Rolls-Royce (Bristol) for the Pegasus engine and BP for its exploration of the Alaskan North Slope Oilfield.

Dr Dent's team developed five processes of gas manufacture, one of which, the conversion of naphtha into towns gas or natural gas substitute, has already earned the Gas Council £0.5 million with a further £2 million to come and more orders expected, principally from America and Japan.

LEVERHULME TRUST

More than a Million

THE Leverhulme Trust spent £1.97 million during 1968–70 on grants to individuals and to charitable institutions. About 65 per cent of the funds available went to educational bodies and £150,000 was distributed in the form of personal studentships and fellowships. And the annual income of the trust, which was set up on the death of the first Lord Leverhulme in 1925, exceeded £1 million for the first time in 1971. The trustees actively encourage projects involving interchange between academics in different countries and about 25 per cent of the total expenditure for the three years was on schemes of this type.

Spending by the trust on what it calls "basic sciences and mathematics" during the three years amounted to £237,000 (Table 1), about 9 per cent more than in 1965–67. Many of the grants went to universities in the form of research fellowships but money was also allocated for the establishment of units within universities. For example, a grant of £31,000 over five years was made to the Institute of Animal Genetics at the University of Edinburgh to help the establishment of an international school of molecular biology; six studentships are to be provided each year for students from Edinburgh to work at the University of Naples and for both lecturers and students from Naples to spend time at Edinburgh. A new unit in social statistics was also set up at the University of Southampton at a cost of £36,000 over four years.

In the applied sciences the chief feature of 1968–70 was the decision of the trustees to make £10,000 a year available for five years to pay for up to five visiting fellowships in industrial biology. The response of individual universities to the proposal was not very encouraging at first but the Science Research Council agreed to administer the scheme because it seemed to fit in with the needs expressed by its own industrial biology working party. Holders of the fellowships—there were two awarded in 1970—spend at least sixteen weeks a year in a university department with the aim of promoting a keener sense of the requirements of industry.

The trust's expenditure on "combined subjects" has included the setting up of courses and fellowships in music and physics, archaeology and metallurgy, and archaeology and physics. Prominent among the grants for medical and dental projects has been the allocation of £60,000 to the Institute of Ophthalmology, University of London, for a unit to study retinitis pigmentosa—a chronic progressive inflammation of the retina.

Research projects in the environmental sciences that have been funded by the trust include a research unit in urban design at the University of Edinburgh and a unit for a study of the location of industry at the University of East Anglia.

Table 1 Expenditure on Science 1968–70

	£ thousand
Basic sciences and mathematics	237.1
Medicine, dentistry and health	272.3
Applied sciences, engineering and architecture	91.1
Environmental sciences	99.6
Combined subjects	8.7
	708.8
	(35 per cent of total expenditure)

SCIENCE MUSEUM

Games People Play

THE Science Museum last week opened an exhibition on scientific toys designed to appeal to both adults and children. The toys range from an eighteenth century orrery to a modern Newton's cradle for frustrated executives which sits inside its glass cage clicking patiently back and forth.

Many of the toys work, and demonstrate various scientific principles from the effects of atmospheric pressure to the use of photoelectric cells. An air fountain with its jet adjustable for height and direction spins coloured pingpong balls in one corner, while at its back a water fountain is operated by thermal pressure. Across the far side a magnetized triangle dances above a triangular layout of magnets as their opposing poles repel it and a mechanical yoyo rolls stolidly up and down. Among the older toys is one of the largest toy steam engines ever made—in Germany in 1906—the dynamo which it powers being used to light the bulbs on a toy Christmas tree. The commentaries round the exhibits include background information and claim that toy manufacturers are rarely far behind scientific advance—a toy do-it-yourself X-ray kit for practice on the family was marketed in Italy early this century before the dangers of X-rays were known.

The exhibition, which will run until March, also includes one or two ideas for re-creating the exhibits in the home. The air fountain, it is suggested, could be constructed with pingpong balls and a vacuum cleaner which can be persuaded to blow rather than suck.

HIGHWAY PLANNING

Marsh's Crystal Ball

THE forum on Public Participation in Highway Planning at the Institution of Civil Engineers last week did little more than to illustrate the gap between the planners and those planned for, and the stuttering inability of public meetings to follow a logical line of thought. Several hundred people filled the Great Hall of the institution to hear questions from the floor answered by four experts in highway planning under the chairmanship of Mr Richard Marsh, Chairman of the Railways Board and ex-Minister of Transport.

The experts were Mr Michael Heseltine, Parliamentary Under-Secretary responsible for motorway and trunk road routes, Mr Frank Layfield, QC, counsel specializing in highway matters, Mr Derrick Beecham, founder of the Homes before Roads campaign, and Mr A. Goldstein, an engineer and member of the Roskill Commission.

Mr Beecham was worried that petrol bombs might be thrown at builders unless politicians listen but the evening's discussion did little more than ignite a few rather damp and well worn squibs.

Any constructive line of argument was defeated by speakers from the floor airing particular grievances or changing the tack of the argument. Complaints were made about inadequate compensation and lack of compensation for people living near motorways. Mr Goldstein warned of the dangers of extensive property blight if detailed plans of all possible routes are published for discussion as some wanted. Mr Beecham and speakers from the floor argued that the public should be consulted before detailed plans are drawn up, and even before the decision is taken over whether the money should be spent on roads at all, rather than on rail.

But do the public want to be involved ? Mr Heseltine said that most people are not interested unless a motorway is likely to plough right through their back garden. Mr Heseltine also argued that from the letters he received, the vast majority of people want new roads.

But while there were plenty of suggestions as to when in the planning process there should be consultation, nobody had much to say as to how this should happen, other than Mr Beecham's suggestion of "some sort of a referendum". How a referendum should be held on the plan of future roads for Greater London was not explained.

Mr Marsh, in summing up, said the meeting showed "what we already knew" —that people are worried about what is being done to the environment. There was, he said, no single and simple answer to the complex problem of road planning. Now freed of the shackles of ministerial responsibility, Mr Marsh assured the meeting that ministers are responsive to public pressure and further that if it builds up, "the government of the day will not change their mind because of it, they will beat (the public) to it and change in advance of it". No doubt, across Parliament Square in Marsham Street, Mr Peter Walker, Secretary of State for the Environment, was busy polishing his crystal ball.

NEW WORLD

Geared for Action

by our Washington Correspondent

NEXT week, between five and ten thousand scientists will converge on Philadelphia for the annual post-Christmas extravaganza organized by the American Association for the Advancement of Science. Part scientific meeting and part public relations exercise for the wonders of science, the annual meeting of the AAAS has for most of the past 138 years served to convey to an admiring public the fruits of scientific research and the flavour of the scientific enterprise. But, like the annual meeting of the British Association, that established order is slowly changing.

For one thing, scientists no longer save up their cherished results to reveal to the world at the annual meeting of the AAAS —that is now the province of scientific journals, or to a lesser extent of more prestigious meetings such as the annual meeting of the American Chemical Society. And, for another, the whole concept of scientists condescendingly handing out fruit from the tree of scientific knowledge to a grateful public (which is in any case indirectly paying for the research and is profoundly affected by it) is anathema to many scientists, and not just those on the far left. Consequently, the AAAS meeting is attempting more and more to look at the complex interrelationships between science and society, and the meetings are increasingly becoming the target of radical scientists who, campaigning under the slogan "science for the people", flamboyantly attack members of the scientific establishment for their elitism and "crimes against the people".

The past two meetings of the AAAS have caught headlines across the United States largely because of the tactics of the radical dissenters, and this year's meeting promises to be no exception. According to one member of SESPA (Scientists and Engineers for Social and Political Action, the organization chiefly responsible for coordinating the dissenters at the past meetings), for example, "the turnout (of radicals) will exceed any one in the past", and according to another, radical scientists will be more in evidence in Philadelphia than they were in Chicago last year.

By their tactics at previous meetings, and widely publicized incidents such as an attack on one radical dissenter by the enraged wife of a biology professor armed with a knitting needle, the objectives of the radical scientists have been obscured and their antics have served chiefly to alienate even many of those scientists who sympathize with some of their objectives. Will this year's meeting see a change in tactics? Herb Fox, a Boston scientist who was active in Chicago last year, and who has been heavily involved in planning SESPA tactics for this year's meeting, said tactics will be chosen to suit the occasion. "We plan to participate in the discussions in a helpful way," he said, but warned "if the AAAS chooses to stop meetings, we shall kick up a stink about it".

For their part, those involved in planning the AAAS meeting point out that they want to encourage participation, and that the menu for the meeting consists of a range of topics from hard science to those where the social content is high. A particular feature of the meeting will be a series of discussions of the role of science in meeting urban problems, particularly in Philadelphia, and there will also be sessions on conflict in Northern Ireland and on "the new radicalism in science". The AAAS even offered SESPA members a hand in planning part of the programme, a move which was rejected by the organization because it might be interpreted as a sign of support for the AAAS, and because it would compromise SESPA tactics at the meeting. Nevertheless, some members of SESPA, Fox included, will take part officially in the meetings, as individuals.

Has the AAAS decided to adopt its own tactics to forestall the protests of the radicals? According to William Bevan, executive officer of the AAAS, the society always prepares a set of operating rules for the chairmen: "We don't play things by ear". But he pointed out that everybody will be free at the meetings to put his own point of view. S. Fred Singer, chairman of the AAAS meetings committee, said that chairmen have been told not to allow bull horns, megaphones and so on into the lecture halls. They have also been given explicit instructions not to close meetings until people have had their say, but that if the meeting becomes unmanageable, they have the power to adjourn—such a decision could be put to a vote, he said.

Singer said that he expects less disruption of the meetings this year, because there will not be so much television coverage—"it is my feeling that many of these people were grandstanding for the television cameras", he said. Fox, however, says "we have done something for the AAAS which they have always wanted to do for themselves, get their name widely known". At least the 1973 meeting of the AAAS will be more removed from the attacks of radical American scientists —the annual meeting is to be held in Mexico City that year.

ARTERIOSCLEROSIS

Another Crusade

by our Washington Correspondent

A MUCH larger national programme aimed at improving prevention and treatment of arteriosclerosis and at stimulating research into its causes has been recommended by a task force set up under the auspices of the National Heart and Lung Institute. Although officials of the institute flatly deny that the report is "a counterbalance or a gimmick to compete with the cancer attack program", the report is aimed at launching a crusade against cardiovascular disease in much the same way as the report of the panel of consultants a year ago launched a crusade against cancer. Moreover, the forthcoming debate about the merits of instituting the report's recommendations will be an interesting lesson in the way Congress and the Administration will set about dealing with large but scientifically and emotionally strong claims from different sectors of biomedical research.

Prepared by a fifteen member task force under the chairmanship of Dr Elliot Newman of Vanderbilt University, and later of Dr Oglesby Paul of Northwestern University, the report calls for a programme which would cost $120 million in the first year and $175 million in the second year above the present funding of $104 million for research and treatment of arteriosclerosis. The basis for this request is that arteriosclerosis is the number one killer in the United States, and that there already exists a strong base of knowledge which would allow programmes aimed at preventing the onset of the disease to have a significant effect on mortality in the United States.

Throughout the Congressional debate on cancer, it was repeatedly emphasized that the disease afflicts about one person in four, but that argument is considerably strengthened when applied to arteriosclerosis, for the task force points out that arteriosclerosis is directly or indirectly responsible for nearly half the deaths in the United States each year. The disease, which is essentially hardening of the arteries caused by fatty deposists on their inner walls, is most prevalent among individuals having one or more of three specific factors—high levels of blood lipids, high blood pressure and cigarette smoking. The task force therefore sees the chief aim of any Federal programme as an intensive effort aimed at public education linked with an expanded research effort aimed at discovering more precisely the links between various factors and onset of the disease.

That arteriosclerosis is caused in large measure by extraneous factors such as diet, habits and perhaps environmental factors can be inferred from the huge discrepancies in the prevalence of the disease among different countries. The United States ranks second in the international ratings and it occurs ten times more frequently there than in Japan. This discrepancy led Dr Charles K. Friedberg, a member of the task force, to suggest last week that if Americans were prepared to alter their diets and stop smoking cigarettes, the incidence of the disease might be cut by 90 per cent.

Among the chief recommendations of the task force are the following:

- Several centres devoted to the study and treatment of all factors of arteriosclerosis should be established in existing hospitals and universities. At present, the task force reports, "the effort is fragmented into small programs at many universities and hospitals. These programs, excellent as many of them are, do not encompass a multidisciplinary attack on arteriosclerosis". Called National Centers for the Prevention of Arteriosclerosis, the centres would be focal points for the study, detection, prevention, arrest and reversal of the disease, and they might be modelled on other mission-oriented government research centres such as the Lawrence Livermore Laboratory or the Oak Ridge National Laboratory.
- Smaller cardiovascular disease prevention clinics should be established within the framework of existing health care. Charged with the task of screening persons to detect those most at risk, the clinics would also serve as a means of collecting together information on the prevalence of the disease and its dependence on different factors.
- The task force also suggests that an Office of Health Education should be established in the National Heart and Lung Institute to serve as a clearing house for information on arteriosclerosis. The office would be partly responsible for public education about the risks associated with, for example, cigarette smoking, and about the advisability of having regular checks of blood pressure.
- As far as research is concerned, the task force suggests that "efforts aimed at primary prevention of arteriosclerosis are not based on adequate information", and that "a vigorous effort of basic and applied research will provide the knowledge required for efficient prevention programs". The research would be carried out primarily in the suggested National Centers for the Prevention of Arteriosclerosis, although the report suggests a large scale programme of applied research to test the so-called risk factor hypothesis. The chief problem with such trials, however, is that they would involve large numbers of patients to be studied over long periods of time, but with the increase in the number of patients under treatment in the national centres, the task force believes that several important questions concerning the causal relationship between factors such as high blood lipid content and high blood pressure can be resolved.
- The task force also recommends that the National Heart and Lung Institute should engage in an expanded programme of basic research to elucidate, for example, factors governing the levels of lipids in the blood, and the mechanisms whereby genetics, hypertension and cigarette smoking affect the formation of fatty deposits on arterial walls.

Dr Paul has described the recommendations of the task force as "a broad, aggressive, realistic program deserving the support of the President, the Congress and of the people". Since the NIH budget is now being negotiated in the Office of Management and Budget, such a report could conceivably have an effect on the institute's funds for next year, and if the report does launch a campaign designed to cut down the incidence of the disease, it is likely to find many friends in Congress. One major difference between this report and last year's report of the panel of consultants on cancer, however, is that the argument is unlikely to be sidetracked into one of organization, because the task force thankfully makes no recommendations for taking arteriosclerosis research outside the National Institutes of Health.

OCEAN MAMMALS

Not Enough Protection

by our Washington Correspondent

UNDER the blind eye of the International Whaling Commission, eight species of whales have been ruthlessly hunted to the verge of extinction. Commercial greed has been the chief factor which has forced the commission's weak and toothless machinery consistently to allow whaling fleets to kill off more whales each year than their rapidly declining numbers can sustain. And, as a monument to bureaucratic controls that allow too much leeway to the commercial interests they are designed to regulate, the International Whaling Commission provides a good example of what not to do. That is one reason why the House of Representatives has chosen to throw out a bill designed to protect all ocean mammals, but whose secondary aim is to "obtain an optimum sustained yield" of the animals for commercial exploitation.

In many respects, backers of the bill were hoist with their own petard, for the bill was brought to the floor of the House under suspension of the rules—a device designed to expedite the passage of uncontroversial legislation which allows no amendments to be brought, and which requires that the bill receives a two-thirds majority to pass. Those who wanted to give the bill more teeth were therefore forced to vote against it, and it received an absolute but not a two-thirds majority.

The bill was voted down essentially because it was felt that the shameful history of marine mammal conservation, which has allowed species after species to become almost if not entirely extinct, requires the taking of more drastic action than simply improving the controls on the giving of licences for hunting the animals. In short, what most opponents of the bill want is a complete moratorium on the killing and harassing of all ocean mammals by United States citizens, and a ban on imports into the country of products derived from these animals (the products are mostly luxury goods).

But the bill brought to the floor of the House by the Committee on Merchant Marine and Fisheries, although it would have led to a moratorium on the taking of some particularly endangered species of marine mammals, also included provisions allowing the Secretary of Commerce or the Secretary of the Interior to grant permits for the taking of other marine mammals. Before such a permit could have been granted, the bill specified that the likely effect on the species would have to be taken into account, and the whole process would be open to public hearing. The granting of such permits would, however, be subject to commercial pressures, and with the glaring example of the International Whaling Commission to hold up, opponents of the measure had enough big guns to shoot it down.

One of the chief reasons that the bill would have allowed the taking of some species of marine mammals is to permit effective management of mammal populations which might become too numerous for their habitats—the situation in the Farne Islands, where the British policy of stopping the killing of seals has led to overcrowding, disease and starvation among the animals was cited as an example. But in the majority of the cases—for example, the wanton destruction of polar bears in Alaska by hunters in the name of "sport", and the commercial exploitation of whales to the point of their extinction—the situation is such that strong controls are essential.

Although the bill has been technically killed by the vote, it may be resurrected and brought back to the House under the normal procedure, thus allowing amendments that would put the necessary teeth into the legislation. That is what most of those who voted it down are hoping.

Safety from Rochschild in Numbers

This is the second in a series of comments on the Dainton and Rothschild reports. The author is Professor C. H. Waddington, Institute of Animal Genetics, University of Edinburgh.

IT is either frivolous or a symptom of a fixation on academia to suggest that reorganization of the research councils is a panacea for curing the difficulties of British high-technology industry. According to the Rand Corporation both pure and applied research amounts to no more than 5 per cent of the total costs involved in American high-technological products, the remainder being devoted to production development and product application in relation to the market. In the Dainton Report (Appendix *D*, Table 2), the research council contribution for the last year quoted (1967–68) was only £57.1 million out of £962.1 million, that is of the same percentage as the USA (though Dainton's total is increased by including defence research and lowered by excluding some of the marketing costs included in the Rand figures). Moreover, although 95 per cent of development has been run on the customer/contractor principle which Rothschild favours, it would seem, in view of recent British experience with advanced aircraft, rocket launchers, nuclear power plants, computer hardware and the like, more in need of radical reorganization than the 5 per cent spent on research. The research councils have every reason to refuse to accept the role of scapegoat. They have done, at a modest fraction of the GNP, a pretty good job—*vide* international comparisons of Nobel Prizes *per capita* as a crude but not negligible index.

Rothschild's recipe is straightforward. The principle is that the people responsible for running the affairs of society, that is the civil servants in executive ministries, know best what new knowledge or expertise is required. This means not only that "the person who has to pay . . . is in the best position to know how much he can afford" (Rothschild, para. 4), but also "the customer says what he wants" (Rothschild, para. 6). This short-circuits one of the traditional levels between customer and contractor. A sick man is usually wise to consult a doctor before going to the chemist for some pills; it is sensible to have an architect between a client and a builder. It is true that Rothschild wants each customer ministry to have a chief scientist (presumably with a staff, though little is said about this). But this has been urged since the end of World War II, with little or no effect. There are three snags.

First, unless the ministry's chief scientist has a fairly large, wide ranging staff, he will simply perpetuate out-of-date scientific orthodoxy. For instance, when I started running a research laboratory for the ARC on genetics in the livestock industry, the ministry, with good scientific advice (from veterinary surgeons), knew just what it wanted—more control over the results of matings between pedigree bulls and cows. Really it wanted something totally different, belonging to a different paradigm—to forget about the Breed Societies, and find out how to operate the Artificial Insemination Centres in terms of hundreds of thousands of matings. But if you were to set up a ministerial science office capable of seeing this far into questions, this would simply be a duplication of the existing research council machinery, with all its expert committees and so on.

Second, this is precisely the pattern of research support in the United States. With the much greater number of people they can call upon for public service, the system of financing research by executive ministeries has been quite successful in tactical detail, but so inadequate on a strategic level that they are moving to greater emphasis on a non-executive agency (NSF) and less project-oriented grants.

Third, scientists capable of something better than run of the mill work may be willing to accept a short term contract if it leaves them free to do what they want; but who is going to buy the Rothschild package which combines insecurity of tenure with official direction?

Thus even if the Rothschild scheme was put into full operation, it would have many disadvantages. Its real dangers are that it will be put into half-operation; the customer–contractor system may be set up before the customer ministries have any effective chief scientists, but only someone in administration who does not see why he cannot do the job well enough. The figures and dates given in Rothschild's Table 4 are presumably intended mainly as a provocative cock-shy, but if anything approaching those transferences were made with the haste suggested, there is a very real possibility that the ARC and NERC will be disrupted, to divert much of their funds straight down the drain.

The Dainton Report is at least less dangerous, but does not go far enough. It would bring Britain halfway to where the USA was in the Kennedy era; with a board of research councils coordinating their activity, rather as the US Federal Council of Science and Technology (FCST) coordinated the American agencies, but still without anything corresponding to the President's Scientific Advisory Committee (PSAC), curtailed though its powers now are.

Finally, a comment which some people will consider frivolous but which is not. The real nature of our research councils is that the person in charge (secretary or what-have-you) has been enabled to operate like a renaissance Pope; his freedom is restricted only by a council and committees whose members he can select himself. It works wonderfully if the Pope is a Medici who likes having his ceilings decorated by Michelangelo. But there is an inherent tendency, in the world as it is, for an enlightened patron, ready to back his fancy for molecular biology in the late forties against the whole biological establishment, to be followed by someone less abrasive and penetrating.

One way of dealing with the situation is to have a fairly quick turnover of heads of councils, with many more people serving for quite short periods on the critical committees—this is what the United States does. We have tended to favour longer periods of service of quite a few people—a major research council may contain only one man in a large field like genetics, and he may stay there for ten years. Then it all depends, is he the right man or not? We have done quite well on the whole, but there is room for improvement. And the obvious step, in this sort of operation, is to have more, smaller, highly personalized research councils, who can pick and choose whom they want to support, and who can be picked and chosen by the scientists who are shopping for a patron.

So long as discussion remains confined to "either Rothschild or Dainton", many of the most attractive improvements will never get a hearing. For instance, what about leaving the research councils with essentially the same financing as at present (except for a few items which are clearly already on a customer/contractor basis), but giving the relevant ministries the chairmanship of some of the appropriate boards or committees which do the donkey work of the councils—the MRC Clinical Research Board, the ARC Animals Committee, and Plants and Soils Committee, and the similar specialist committees in NERC? It would be necessary to strengthen the scientific sections of the ministries to provide them with people who could even chair and make worthwhile contributions to such bodies; but it would provide a means of mutual education between the research and executive interests, and this is, I suggest, what we need, rather than dominance of either one over the other.

NEWS AND VIEWS

The Earth's Cores

THE inner core of the Earth has for too long lived in the shadow of the outer core. A great deal is known about the outer core: it is liquid, it has a radius of 3,480 km and it is almost certainly made mostly of molten iron. The inner core was detected because some seismic energy was recorded by seismographs lying between 105° and 143° from earthquakes. In the absence of an inner core these instruments should have lain in the shadow of the core and have received no energy. It seemed impossible that the energy was diffracted into the shadow and it was postulated that there was an inner core with a radius of 1,200 km, from the surface of which the seismic waves were reflected.

Having found or suspected that the Earth has an inner core it was natural to enquire whether it is solid or liquid. There was a certain convenience in having it solid, because it could then be supposed to be made of the same material as the outer core and to be solidified by pressure. This was an easier view to explain to undergraduates than the alternative that the two cores were composed of two immiscible liquids. Are there immiscible liquids at high pressures and temperatures ? Maybe not, but who can tell? It is possible that a liquid can be formed from molten iron by collapsing the partially filled D-shell of extranuclear electrons ; maybe it will not mix with ordinary molten iron. It would seem that the matter could easily be settled by showing that both compressional and distortional waves can travel through the inner core ; to transmit distortional waves is an essential property of a solid. The distortional waves have not in fact been found, but the seismogram fanciers are not willing to say that they are absent. In these circumstances, those people not immediately concerned mostly concluded that very little was known about the inner core and that it was best left to the experts till its properties became clearer.

In this issue of *Nature* (page 465) Dziewonski and Gilbert provide strong evidence for the solidity of the inner core. The Earth possesses "normal modes" which are excited by earthquakes. To deduce the structure of the Earth from them is rather like deducing the structure of a piano from the noise it makes when thrown downstairs. It is possible because there are already rather good models of the Earth derived from seismic travel times. Dziewonski and Gilbert have picked out particular kinds of vibrations which have an appreciable part of their energy (up to 20 per cent) in the inner core and the frequency of which therefore depends markedly on its properties. The results are entirely compatible with a solid inner core and Dziewonski and Gilbert believe that no model with a liquid inner core can satisfy all the data.

Dziewonski and Gilbert's model is important. If the transition from the inner to the outer core is a transition from the solid to the liquid forms of a single material, then the boundary must be at the melting point and a constraint is put on the thermodynamics of the Earth's interior. That the boundary is at the melting point is an essential assumption in an argument put forward by Higgins and Kennedy (*J. Geophys. Res.*, **76**, 1870 ; 1971) which suggests that the outer core is stably stratified. If this is so the large-scale steady motions usually postulated as constituting the dynamo that produces the Earth's magnetic field are presumably not possible (for a possible escape from this misfortune, see Bullard and Gubbins, *Nature*, **232**, 548 ; 1971).

The very existence of an iron core suggests ideas on the early history of the Earth. It is unlikely that the Earth accumulated in two stages, first particles of iron forming the core and then particles of silicate forming the mantle. Whatever the exact mechanism it seems likely that at the start the particles of iron and silicate were mixed up. If the accumulation were very rapid or if it took place in a very opaque atmosphere, the energy of impact would cause the particles to melt and could lead to separation of the core beneath the lighter mantle just as iron separates from slag in a blast furnace. Alternatively, if the rate of accumulation is slow the gravitational energy of each incoming particle will be radiated away and the Earth will accumulate as a solid with a temperature of a few hundred degrees. It is then possible that radioactivity will cause melting and separation of the core after a time of the order of 10^8 years. There are therefore two possible views about the history of the core ; it could have formed as the Earth accumulated or its formation could have been a subsequent event. The second is the fashionable view, though it cannot be said that the arguments in its favour are conclusive.

On page 463 of this issue, Oversby and Ringwood argue for the first view—the very early formation of the core. They point out that the formation of the core would remove lead from the mantle and decrease the Pb/U ratio. The lead at present in the mantle is partly that left after the formation of the core and partly that produced by decay of uranium and thorium in the mantle. If the original isotopic composition of the lead incorporated in the Earth, the present composition of the lead in the mantle and the proportion of lead removed in forming the core are known, then, according to Oversby and Ringwood, the time of formation of the core can be found. These quantities can, with varying degrees of plausibility, be said to be known, and the result favours an early formation of the core.

Details of the argument will be awaited with interest. The formation of the core while the outer part of the Earth was solid would have been a cataclysmic event (there is a large release of energy) ; it must have occurred before any of the rocks now at the Earth's surface were formed. The ages of the oldest known rocks have been increasing and are now about 3,980 million years. The margin between this figure and the age of the Earth (4,550 million years) is becoming uncomfortably narrow and early core formation seems, on these grounds, desirable.

Cooperation between B and T Cells

THE experimental evidence which underlies theories for the function of B and T cells—lymphocytes which originate from the bone marrow and thymus respectively—derives from mice and latterly rats. Some support can be gleaned from various immunodeficiency syndromes in man but the picture presented is, as always with nature's uncontrolled experiments, rather confusing. Indeed, those immunologists who work with sheep find the whole notion of B and T cells unhelpful. But from all these different opinions may arise the heat to temper something solid which can actually be used in rational manipulations of immunological processes. On page 454 of this issue of *Nature*, H. W. Kreth and A. R. Williamson present a hypothesis for the mode of interaction of B and T cells which, if it can be substantiated, will present a valuable way of thinking of one of the associations between lymphoid cells.

If small numbers of spleen cells, from mice which have been immunized with DNP–BGG (dinitrophenol coupled to bovine gamma globulin), are transferred into irradiated syngeneic recipients and the antigen is injected again, production of anti-DNP antibody can be noted. The antibody produced in the original host is heterogeneous but in the secondary host the heterogeneity is sometimes much less. Furthermore, if spleen cells from the secondary host are transplanted into a third host (along with antigen) not only can the immune response be maintained but the exact quality of the antibody is reproduced.

This type of experiment has been said to lead to the production of clones of B cells capable of producing homogeneous antibody. Some reservation should be expressed about the "clones" because their identity is said to be established by their protein products rather than by, say, a cytogenetic marker. The assumption is here made that it is unlikely that cells of two different lineages should produce the same protein molecule; in other words, specific immunity is neither infectious nor polyphyletic. But aside from these considerations the capacity to produce the homogeneous anti-DNP antibody has been shown to depend on the activity of B cells. There has also been revealed a requirement for carrier-primed T cells. For example, if the spleen cells used to transfer the capacity to produce anti-DNP antibody are incubated, on transfer, with anti-θ antiserum (to eliminate T cells) in the presence of complement the immune response fails. An anti-θ depleted spleen cell population can be restored to its usual functional capacity by the addition of carrier primed syngeneic spleen cells. This type of experiment which implicates the T cell in relation to the anti-carrier and the B cell in relation to the anti-hapten response has led to the hypothesis that interaction between T and B cells involves an antigen bridge. The T cell is imagined to be at the carrier foundations of the bridge proffering the hapten in a particular manner to the B cell on the other side.

In earlier experiments it has been shown that attempts to elicit anti-DNP antibody formation, on transfer, by the use of DNP bound to a different carrier (for example, ovalbumin, OA) are unsuccessful. This suggests that the T cell, which is responsible for the anti-carrier response, makes a specific contribution to the immune process. Kreth and Williamson reasoned that this may not be so. They offer in evidence the fact that if spleen cells from an animal producing a homogeneous anti-DNP antibody are transferred to an irradiated recipient along with DNP bound to a heterologous carrier (DNP–OA instead of DNP–BGG) a secondary anti-DNP antibody response results if unprimed AKR spleen cells are added to the inoculum. Kreth and Williamson argue that the reaction of the T cell component of the AKR spleen populations against the CBA (B) cells in the immune syngeneic spleen cell population provides the necessary bridges and non-specific stimulation which are required to promote anti-DNP antibody production in the presence of DNP bound to any carrier. With this experimental finding as the basis of their case they go on to adduce a general theory for interaction between B and T cells.

Kreth and Williamson suggest, following Burnet, that cells have a surveillance function in relation to other cells. B cells can firmly bind antigens to specific receptors on their surface but beyond that point they may need some further stimulus to react. Wandering T cells, finding the foreign material bound to the B cells, form some link with the altered B cell, and produce a mitogenic stimulus which triggers the further response of the B cell to the bound antigen. In their experimental studies Kreth and Williamson envisage that by providing an artificial difference between the interreacting B and T cell populations they exaggerated the kind of response which normally occurs between B and T cells. They cite the evidence that T cells are responsible for effector function in cell-mediated immunity and they feel that their postulated role in B–T cooperation systems is consistent with this aggressive potentiality.

Perhaps the weakest point of Kreth and Williamson's theory is the lack of any suggestions about the "appropriate receptors" which are said to enable the surveying T cells to recognize foreignness on the surfaces of other cells. This failing, however, is not unique when the discussion turns to interactions between such complex matrices as mammalian plasma membranes.

Righting the Applecart

THE discovery during the past year of pulsating X-ray sources with little or no easily detectable radio and optical emission has upset the pulsar applecart. It has become obvious that some phenomenon other than the accustomed pulsar models is active in these energetic sources. For the present the questions are what sort of phenomenon, and is one extra phenomenon sufficient to account for the observations ?

Henriksen, Feldman and Chau (Queen's University, Ontario) believe they have answered the first of these questions with their model, which they apply to Cen XR-3 on page 450 of this issue of *Nature*. The general applicability of the model has yet to be confirmed, but it could well turn out that the application of this model to other pulsed X-ray sources will answer the second question too.

Apart from the pulsations themselves, several of the newly observed sources are characterized by emission which can be interpreted in terms of black body radiation or by thermal bremsstrahlung. Henriksen, Feldman and Chau favour a black body spectrum, and in fact the data on the recently discovered X-ray pulsar Cir XR-1 seem to be a fractionally better fit to the black body spectrum than to thermal bremsstrahlung. Henriksen, Feldman and Chau's work may also be relevant to the X-ray source GX 340+0 which has recently been determined to have in all probability a black body spectrum, although there is no evidence so far that GX 340+0 is pulsating. This is the only object so far for which the resolution is adequate to distinguish between the black body and thermal bremsstrahlung models.

The model by Henriksen, Feldman and Chau is based on the generation of heat in the crust of what they call a wobbling neutron star, and the periodicity of about 5 seconds that is observed in the X-ray data is attributed to the free nutation period. It seems too much to hope, however, that all the pulsating X-ray sources will fit neatly into this scheme. Although knowledge of the characteristics of pulsed X-ray sources is still in a confused state, two classes of sources are emerging. On the one hand are the sources Cen XR-3 and NP 0532 (the pulsar in the Crab Nebula which is detectable at frequencies from the gamma ray to the radio band), which are characterized by well-defined periodicities, implying that some phenomenon involving the whole star—such as rotation—is involved in the timing mechanism. On the other hand, however, are sources such as Cyg X-1 and Sco X-1 which seem to emit short trains of pulses whose periodicities can be different from one pulse train to the next. Some periodic phenomenon involving only the atmospheres of the objects seems the likeliest explanation that will allow this kind of irregularity.

Nor is this to say that further sources in the first class will be susceptible to the treatment of Henriksen, Feldman and Chau. For the present, other more established views based on the population of radio pulsars seem to give a good account of the X-ray emission from NP 0532, and such models would also presumably work for PSR 0833-45 if and when X-ray emission is detected from this other fast pulsar. For the time being, then, the deep pulses from Cen XR-3 containing 70 per cent of the radiated power (2–6 keV) seem to be in a class of their own.

GX3+1

Two Candidates

ALL but two possible candidates for the optical counterpart of the X-ray source GX3+1 have been eliminated by two successful lunar occultation experiments, which have reduced the uncertainty in its known position by a large factor. The Skylark rocket flights which have produced this improvement were carried out from Woomera for the University of Leicester group (on September 27 this year) and for the University College, London, group (on October 24). It was necessary to take advantage of the rare occultation of the source by the Moon (see *Nature Physical Science*, **233**, 106; and **234**, 2; 1971) because in the best error circle available previously there were a great many stars, but none of them had a sufficiently striking spectrum to make it a likely candidate as an optical counterpart of the X-ray source.

Both groups have now completed the reduction of their data, and their results have been combined to give an improved fix on GX3+1. This fix is so good that the exact positions of faint stars in the area have had to be redetermined for comparison with the X-ray data. Two possible candidates have been found, lying one either side of the error box and close to RA 17h 44m 51.5s dec −26°33′50″. Either GX3+1 is associated with one of these stars (numbers 14 and 15 in the notation of Kunkel *et al.*, *Astrophys. J. Lett.*, **161**, L169; 1970), or it is fainter than 18th magnitude and lies between them, or it is fainter than 21st magnitude and lies somewhere else in the error box.

Interaction between HL-A Antigen Determinants

HL-A ANTIGENS, like other genetically based polymorphisms in man, have acquired a mystique which has tended to isolate discussion to the habitués. The meaning of "HL" is itself a matter of some doubt. By usage it has come to be accepted as an abbreviation for "human leucocyte", but its propositors (see Amos, *Science*, **159**, 659; 1968) meant it to stand for "human histocompatibility locus".

It seems that HL-A antigens are controlled chiefly, but perhaps not exclusively, by two closely linked genetic loci often known as the first and the second. At each locus a number of alleles are recognized the activity of which results in the synthesis of various antigens designated (for the most part) HL-A1, HL-A2 and so on. Unfortunately, consecutive numbers can relate to antigens associated with different loci; for example, HL-A8 is determined by locus 2; HL-A9 is determined by locus 1. This muddle has arisen because the antigens and their controlling genes were not discovered in a nice neat sequence. The antigens are usually recognized by the use of specific cytotoxic or complement-fixing antisera used on leucocyte or platelet populations *in vitro*. A report by Legrand and Dausset in next Wednesday's *Nature New Biology* (December 29) reveals an interesting facet of these tests.

The leucocytes from a single human individual can carry four different antigens determined by the first and second loci, that is, when heterozygous at both loci. Legrand and Dausset took the cells from such an individual (HL-A3, 5/10,12; 3 and 10 determined by genes at the first locus, 5 and 12 by genes at the second locus), and incubated them with a selected antibody (say anti-HL-A3) in the absence of complement. When the cells showed no further capacity for the absorption of anti-HL-A3 antibody they were incubated with one of the other three relevant antisera and the specific cytotoxic effect of the resulting supernatants was quantitated. By reference to the gene loci it can be said that sequential incubation with anti-HL-A3 and with then anti-HL-A10 is an allelic combination, anti-HL-A3 followed by anti-HL-A5 is a *cis* combination, and anti-HL-A3 followed by anti-HL-A12 is a *trans* combination. There are four of each kind of combination of different antisera. Legrand and Dausset found that when the antigens were attacked in the *cis* combination incubation with the first antiserum inhibited the absorption of the second antiserum. Further studies on genotyped patients established that this was a general rule.

This finding that there can be interference between combining sites on the cell surface which are determined by "adjacent" genes on a chromosome is in agreement with previous studies with mouse (H-2) histocompatibility antigens. The inference to the geneticist, as indicated by Legrand and Dausset, may be that two HL-A genes in the *cis* position cooperate in the building of a single molecule. To the transplanter it may well be that if an antibody to a particular antigen can be elicited which can block combination of antibody with another antigen (in the *cis* position), certain typing mismatches may be of no consequence. It would also be of interest to determine whether the inhibiting antibody prevented attack by cytotoxic cells.

THE ARCTIC

Peppering of Pingos

from our Geomagnetism Correspondent

ARCTIC seas are not, for obvious reasons, heavy shipping areas, with the result that bathymetry is poorly known and possible hazards to shipping are almost completely uncharted. The discovery of oil in Alaska and the use in 1969 of the SS Manhattan to test the feasibility of waterborne access to the oil fields have led, however, to an extensive programme for charting of northern seas and the investigation of the seafloor, chiefly by Canada. As a result of such studies in the Beaufort Sea, Shearer *et al.* (*Science*, **174**, 816; 1971) are now able to report their discovery of a feature of the ocean floor which is of both practical and academic interest—the pingo.

The road to the discovery was actually begun by an observation taken during the voyage of the Manhattan to Prudhoe Bay in 1969. At one point during passage through the Beaufort Sea (actually about 120 km north-west of Atkinson Point, Northwest Territories) there occurred a rapid shoaling which led to a reduction of water depth from 49 m to 23 m within a horizontal distance of 200 m followed by an equally abrupt return to the original depth. The region including this topographic feature has since been the subject of a more detailed bathymetric, sonar, gravimetric, magnetic, seismic and sampling survey which has led to the discovery that the original feature—nicknamed the "Admiral's Finger"—is far from unique. The whole area is in fact peppered with similar underwater mounds rising from an otherwise smooth seafloor. Each such mound is usually irregularly and asymmetrically shaped with one side steeper than the other. The base diameter averages 400 m, the average elevation is 30 m, and in most cases a moat up to 10 m deep surrounds the base. Within the 5,000 km^2 survey area seventy-eight mounds were discovered scattered apparently at random and with depths of water above their summits ranging from 15.4 to more than 45 m.

In a region where shipping is already subject to the iceberg hazard, the existence of mounds scattered randomly around the seafloor is, of course, a matter of severe practical importance. Academic interest, on the other hand, centres on their cause. The mounds do not seem to correlate with any other of the geophysical parameters measured simultaneously with bathymetry. The magnetic field, though measured to the nearest gamma, indicated no anomalies in the sub-bottom structure; nor did the gravity field measured to the nearest milligal. Moreover, seismic studies showed the sub-bottom reflectors to be more or less horizontal beneath the mounds.

What are these mounds? Basing their argument largely on a comparison between the morphology of the mounds and that of similar structures found 120 km to the south on the Tuktoyaktuk Peninsula, Shearer and his colleagues suggest that the features are pingos—hills which have a central core of ice. This being the presumed case, all that needs to be decided is when and how they were formed.

There seem to be two main possibilities—the terrestrial origin and the submarine origin. By the first the mounds are the submerged portions of pingos formed above sea level during the last glacial maximum when, as a consequence, the sea was about 100–150 km below its present level. The exposed portions of the present Beaufort Sea floor, outside the ice margin but subject to permafrost, would have contained lakes which did not freeze completely to the bottom. Some of these would subsequently have been shoaled either by infilling or draining to produce a body now defined as a pingo. The problem with this idea, however, is that it is difficult to imagine that subsequent wave action would not have eroded the pingos away by now.

The second possibility is that the mounds are pingos "in the genetic sense"—formed in the submarine environment since the postglacial rise in sea level. If the lakes in the previous example were not shoaled before the inundation by seawater, the remaining fresh lakewater would have to mix with seawater when such inundation took place. In this case the unfrozen water of the lake would come under the thermal influence of the overwhelming sea. Because the seawater temperature was almost certainly below −1° C—that is, lower than the temperature of the lakewater—the 0° C isotherm below the old lake would have moved downwards into the sediment thereby causing a freezing of the interstitial water and the consequent upheaval of the overlying material.

Of the two theories Shearer and his colleagues favour the second because of the erosion problem. They then go on to estimate the minimum age of a mature pingo by estimating the time required to freeze the depression of the permafrost layer formed in the insulated region beneath the original lake bed. Making reasonable assumptions about the size and shape of the depression, the thermal conductivity of the sediment, the surface temperature and geothermal heat flow, they come up with the figure of 5,000 years. In other words, on this estimate—and if pingos are of submarine origin—the postglacial rise in sea level must have taken place before 5,000 years ago.

A New Magnetic Reversal at 12,500 Years?

IN next Monday's *Nature Physical Science* (December 27) Mörner *et al.* report their discovery of a reversely magnetized sediment section about 12,500 years old. The section in question is part of an oriented core, 14.5 m long, from Gothenburg, south-west Sweden, which spans the time range 12,600 years to 8,600 years before present (from the early Ågård Interstadial to the mid-Boreal)—and there is little doubt that this dating is correct. The stratigraphy of southern Scandinavia is well known and a well dated climatic zone system has been determined for this range of time. For the Gothenburg core both climatic and stratigraphic dating agree well.

The core contains thirteen stratigraphic units, only the lowermost (earliest) sample (layer 13) of which is reversely magnetized. The boundary between units 13 and 12 is the boundary between the Ågård Interstadial and (above) the Fjärås Stadial and has previously been dated at 12,400 years old. Thus in the view of Mörner and his colleagues 12,400 years represents the upper boundary of a reversal event in the archaeological section of the Brunhes normal epoch.

The palaeomagnetic measurements, including magnetic cleaning up to 200 oersteds, show that the remanent magnetizations are stable—but normal for units 1–12 and reversed for unit 13. Mörner and his colleagues are thus well supported in their report that reversely magnetized material exists in the late Weichselian. But the contention that this represents a genuine field reversal is much less secure. For one thing no search for self-reversal characteristics is reported; and no confirmation from other sections is yet available. Moreover, although the probability that many short events remain to be discovered is now widely accepted, it is equally clear that the definition of short events is likely to be difficult—partly because a given short event will tend to be recorded less often, partly because such events are hard to distinguish from the spurious effects unavoidable in the Earth sciences, and partly because if self reversal operates at all it is likely to manifest itself exactly in this small scale situation.

The best known, and better documented, short reversed event alleged to lie in the Brunhes is, of course, the so-called Laschamp event; and this is far from being widely accepted as valid. Under these circumstances it may seem a little premature to name the new, apparent event.

PROTEINS

Enzyme and Means

from our Molecular Biology Correspondent

FRIEDEN's group in particular has helped to establish bovine glutamate dehydrogenase as an archetype for a ligand-controlled enzyme. Moreover, a great number of physical methods have been brought to bear on the problem of identifying the various enzymatic manifestations with physical changes in the protein, in respect particularly of conformation and association state. The enzyme possesses both glutamate and alanine dehydrogenase activities. The first is activated by ADP, which is also known to promote the well known propensity of the molecule to associate indefinitely to a highly polymerized form. GTP, on the other hand, tends to dissociate the enzyme, while inhibiting glutamate dehydrogenase and stimulating alanine dehydrogenase activity. The evidence has not favoured the original conjecture that the glutamate dehydrogenase activity was associated solely with the polymer, but the issue has only now been conclusively settled.

R. Cohen has devised a method of observing the sedimentation of an enzymatically active species in the ultracentrifuge in minute concentration. It involves the use of a substrate, which on exposure to the enzyme causes an adsorption band to appear or to vanish, according to whether the substrate or the product is the accessibly absorbing species. A layer of enzyme solution is allowed to sediment in a band-forming centrepiece through the substrate solution. The ins and outs of the technique are described by Cohen and Mire (*Eur. J. Biochem.*, **23**, 267 ; 1971), and it clearly has great advantages, including the low requirement in material, the possibility of observing the enzyme in question in a protein mixture, and of operating at protein concentrations so low as to be otherwise non-existent from the viewpoint of the ultracentrifuge. Diffusion coefficients can also be determined. In the accompanying article (*ibid.*, 276) Cohen and Mire show results for a series of enzymes, including some not yet isolated in pure state, and determine the sedimentation coefficients of the active oligomeric states. There are no surprises, and for glutamate dehydrogenase in particular both glutamate and alanine dehydrogenase activities sediment at about 13S, which corresponds to the unassociated hexamer, which, according to hydrodynamic analyses of the association equilibrium, is the expected state at such low concentrations.

Arnold and Maier (*Biochim. Biophys. Acta*, **251**, 133 ; 1971) have isolated, crystallized and characterized glutamate dehydrogenase from rat liver. In terms of its sedimentation coefficient, and its reactivity towards antibodies directed to the bovine enzyme, it is indistinguishable from the latter. There is, however, no trace of the self-association behaviour. It seems by no means unlikely that this phenomenon is in fact a red herring so far as the physiological function of glutamate dehydrogenase is concerned.

Another issue which has been a matter of dispute for some time is whether glutamate dehydrogenase has one, or more than one, functionally important binding site per monomer for its coenzyme, NAD or NADH. The presence of two sites has now been inferred from circular dichroism measurements by Jallon and Iwatsubo (*Biochem. Biophys. Res. Commun.*, **45**, 964 ; 1971), closely followed by Koberstein and Sund (*FEBS Lett.*, **19**, 149 ; 1971). NADH, when it binds to the enzyme, greatly enhances optical activity, in the form of a sizable positive Cotton effect in its near-ultraviolet absorption band. In the presence of the modifying ligand, GTP, or of zinc ions, which exert the same kind of functional directing effect, this Cotton effect suffers an invasion and enhancement. A similar effect is brought about by the substrate, glutamate, in the presence of NADH. In the quaternary complex with substrate, NADH and zinc, however, the amplitude of the Cotton effect shows a further increase.

Observation of the ellipticity as a function of the NADH concentration in the presence or absence of substrate and activator indicates that the cofactor does indeed attach at two sites. The first and stronger is associated with a Cotton effect, that is modified in sense and magnitude by GTP or zinc ions, both of which may well interact directly with the NADH, its binding site, or both at once. The diphosphate, NADPH, will bind at only one site. ADP, when added to the ternary complex, chases the second NADH from its site. The suggestion of Jallon and Iwatsubo is that the second NADH site is made manifest by a conformational change resulting from the binding of the effector ligand.

PHOTOBIOLOGY

Light and Life

from a Correspondent

THE use of damaging radiation on biologically active molecules was the central topic of a joint meeting on December 7 at the Royal Institution in London of the British Photobiology Society and the Society of Chemical Industry. It was clear from the remarks of Dr A. Knowles (University of Sussex) that low energy solar radiation not absorbed directly by a biological system can be very destructively utilized in a photodegradation reaction if an appropriate sensitizer is present. Under most conditions the triplet state

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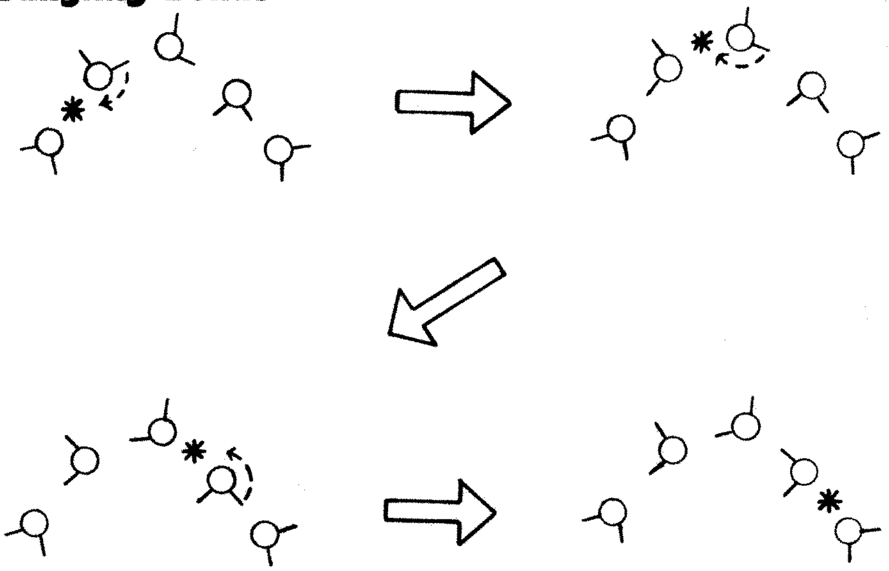
Dangling Bonds



IN next Monday's *Nature Physical Science*, Dr A. P. Hinton of the National Institutes of Health, Bethesda, presents computer calculations of the relaxation of the electric dipole moments of water in terms of a point defect model. The model is based on the fact that although the O-H--O bond is flexible there are some O-H groups that do not participate in a hydrogen bond.

These dangling bonds are considered by Hinton as being analogous to a crystalline point defect. The figure here shows a schematic representation of the migration of such a dangling bond by means of sequential reorientation of water molecules.

of the sensitizer, which can be a dye molecule, is thought to interact with the substrate in one of several ways including direct energy transfer or by way of a second reactive species such as singlet oxygen. Dr Knowles indicated that his studies on the photoinactivation of nucleotides could be explained by a free radical hydrogen abstraction process which forms peroxides.

Whereas most research on photochemical mechanisms has involved the use of isotropic fluid solvents, there were two reports at the meeting that suggested the need for new studies using reaction media which more closely simulate natural conditions occurring *in vivo*. Dr M. Weese (Davy Faraday Laboratory, Royal Institution) told of her work on photoactivated electron transfer from chlorophyll *a* to quinone in a rigid lecithin matrix. The phospholipid solvent allows this reaction to be investigated under conditions close to that found in the chloroplast: high concentrations of reactant which are constrained in their diffusional motion. The kinetics of the electron transfer process indicate that the reaction occurs between pairs of nearest neighbour molecules and the speed of the reaction is quite sensitive to the shape of the quinone used. Another atypical reaction medium was discussed by Dr F. McCapra (University of Sussex) who indicated that the efficiency of chemiluminescence can be strikingly increased when the reaction is allowed to proceed in solvents which form micelles.

The general feeling of the participants was that a better understanding of these reactions could result in the selective photomodification of certain biological systems. The use of light energy to inactivate viruses or to destroy individual amino-acids of a protein was discussed. Professor F. R. Whatley (University of Oxford) pointed out that paraquat, a bipyridylium salt, only showed herbicidal activity on green plants in the presence of light. This may mean that incident radiation and an appropriate sensitizer can be used to limit the effective life of these growth regulating substances.

MESSENGER RNP

Informofers

from our Cell Biology Correspondent

ONE of the more notable contributions made by Russian molecular biologists has been the investigations of Georgiev and his associates into the state of messenger RNA and its precursors in the nuclei of eukaryotic cells and the transport of messenger from nucleus to cytoplasm. In 1968 (*J. Mol. Biol.*, **33**, 251 ; 1968) Samarina *et al.* presented evidence which indicated that the DNA-like RNA in rat liver cell nuclei is complexed with protein particles to form a ribbon-like structure with a series of 200 Å, 30S ribonucleoprotein structures along its length; they proposed the name informofer for these 30S protein particles, anticipating that this protein would prove to be involved in the transport of segments of DNA-like RNA from the nucleus to the cytoplasm where it might act as messenger. Lukanidin, Aitkhozhina, Kulguskin and Georgiev (*FEBS Lett.*, **19**, 101 ; 1971) now report a simple procedure for the isolation of intact unaggregated informofer particles which are free of RNA.

By dialysing nuclear ribonucleoprotein aggregates against 2 M NaCl and then separating the products of dialysis by centrifugation through sucrose gradients Lukanidin *et al.* were able to isolate the free informofers. When exposed to urea each informofer dissociates into its subunit polypeptide chains, over 90 per cent of which are identical and have a molecular weight of about 40,000. Intact informofers readily interact *in vitro* with DNA-like RNA to reform the ribbon-like aggregates which, with a series of 30S informofers strung out along an RNA chain, superficially resemble polysomes.

With Williamson, of the Beatson Institute in Glasgow, Lukanidin and Georgiev (*ibid.*, 152) have compared the informofer protein with the protein to which the messenger RNA moiety of cytoplasmic ribosomes is associated. Their aim was to discover whether or not informofer protein is transported across the nuclear envelope and into the cytoplasm with messenger RNA. To avoid the possibility of artefacts stemming from the leakage of informofer protein from the nucleus during the experimental manipulations they used reticulocyte polysomal ribonucleoprotein, for reticulocytes lack nuclei. Polyacrylamide gel electrophoretograms of informofer protein and the protein associated with globin messenger RNA reveal that the two classes of protein are very similar but definitely not identical. It seems therefore that informofer protein probably does not cross the nuclear envelope or, if it does, it is modified.

The disturbing possibility that the protein found associated with the messenger moiety of isolated polysomes is an adsorption artefact, generated as the polysomes are extracted, is shown to be highly unlikely by the recent experiments of Olsnes (*Europ. J. Biochem.*, **23**, 248 ; 1971). By a series of reconstruction experiments he has shown that artificial ribonucleoprotein complexes produced by incubating nuclear DNA-like RNA with cytoplasmic extracts are less stable than the messenger containing ribonucleoprotein complex isolated from polysomes; the artificial complex, for example, does not survive centrifugation through sucrose gradients. Olsnes concludes therefore that the polysomal, messenger ribonucleoprotein is probably not an artefact but exists *in vivo*.

Ribosomes and tRNA Recognition

IT is often convenient to imagine the ribosome as a simple piece of cellular machinery the job of which is nothing more than to catalyse the formation of peptide bonds between a peptidyl-tRNA and an amino-acyl-tRNA which have reached juxtaposition as they decode a messenger. But that is a gross oversimplification of the ribosome's role in protein synthesis as investigations stemming from the discovery that the antibiotic streptomycin interferes with the codon-anticodon recognition process have amply proved. Indeed, Gorini suggests in next Wednesday's *Nature New Biology* (December 29) that the ribosome plays a considerable part in screening incoming transfer RNA molecules before and at the same time as they interact with messenger RNA.

Gorini has obtained strains of *Escherichia coli* which have mutated ribosomal proteins and has studied the effects of these mutations on the misreading of the genetic code and the suppression of nonsense codons by different species of suppressor tRNAs. The results of his experiments lead Gorini to suggest that there exists "a ribosomal screen which allows the binding of tRNA to the ribosome but antagonizes tRNA from reaching the stage of codon-anticodon interaction". The extent to which any particular species of tRNA participates in protein synthesis will as a result depend not only on the strength of the codon-anticodon interaction but also on the ease with which the tRNA can penetrate the ribosomal screen.

A complete understanding of precisely what happens during protein synthesis depends eventually, of course, on elucidating the three-dimensional structure of transfer RNA molecules and of ribosomes and messengers and finding out how mutations change the structure and function of these components. Little progress has so far been made with this structural analysis but as Kurland and Green report, also in next Wednesday's *Nature New Biology*, strains of *E. coli* with mutationally altered ribosomal proteins, which differ from their wild-type counterparts in the strength with which they interact with ribosomal RNA during the assembly of ribosomes, can be isolated by screening cells that have reverted from a state of dependence upon streptomycin.

Twenty-five Years of the South African CSIR

S. MEIRING NAUDÉ
Past-President, South African Council for Scientific and Industrial Research

In this article, Dr Naudé examines the development of the South African Council for Scientific and Industrial Research and highlights the underlying principles which guide it.

THE South African Council for Scientific and Industrial Research (CSIR) was inaugurated on October 4, 1945, and has thus been in full operation for more than twenty-five years. The two men primarily responsible for the establishment of this organization were the late Field-Marshal J. C. Smuts and Sir Basil Schonland—both Fellows of the Royal Society. Their vision, as embodied in the basic pattern of organization, has stood the test of time remarkably well.

Laboratories and Institutes

The president of the council is also the full-time chief executive officer, and is supported by a deputy president and three vice-presidents. The national research laboratories or institutes set up by the council, each with its own director, are similar in many respects to those of the former Department of Scientific and Industrial Research in the United Kingdom. A distinctive feature is that ten of these are located on one site on the outskirts of Pretoria, together with central technical and information services. There are three in Johannesburg and one in Port Elizabeth.

There are four industrial research institutes, which are patterned on the British research associations; a distinctive feature is that all four are associated with universities. Co-operative industrial research is also catered for by groups and units operating within the framework of the national laboratories and institutes but identified with, and supported by, the industries they serve. Contract research for private firms has been developed successfully by the national laboratories and institutes, though their chief sponsors are government departments and public bodies.

From the outset, the CSIR was given responsibility for "exploring and developing the whole field of medical research". This it did through a system of support for research units, groups and projects as well as *ad hoc* grants. This provided for the continuity of research, built up around individuals of outstanding ability, and avoided many of the problems of institutionalization. This activity, however, became the responsibility of the South African Medical Research Council which was established in 1969.

University research in other fields (excluding agriculture, geological survey and the human sciences) has been developed in much the same way. Funds provided for this purpose have been kept separate from the funds available to the research organization of the CSIR itself, and by drawing academic staff into the procedures for evaluating applications and adjudicating awards, they have shared in the invidious task of allocating funds which are inevitably less than the demand. By these means, justice has been seen to be done.

There has of course been the inevitable disagreement about the role of the national laboratories and institutes in the field of basic research. This has not deflected the CSIR from its policy that the continued health of its own research requires a balance between applied and basic research. The council is assisted in maintaining the quality of research through a system of project steering committees, advisory committees and specialist advisers. Relevance of research is achieved by insisting that a project should, where possible, have a potential customer and by allowing projects to grow in relation to the extent of support or demand for sponsored work. Clearly there can be no hard and fast rule about this, but in practice it turns out that approximately 50 per cent of the revenue is derived from sponsored work.

This figure is somewhat misleading because two institutes, the National Institute for Road Research and the National Institute for Defence Research, are fully supported by the government departments concerned and not by direct Parliamentary appropriation. The particular merit of this arrangement is that, although the budgets of these institutes are controlled by these departments in terms of, for example, relevance of research programmes in relation to practical results, the research is directed by the CSIR. To a lesser extent, important programmes or projects in other institutes are sponsored in the same way by industries (on a cooperative basis) or by public bodies.

In retrospect it is a source of some satisfaction to find that the policy of establishing small centres of excellence within the national laboratories—either in new fields of research or in relation to particular fields of application—has paid off even better than we might have hoped. Two examples will suffice by way of illustration.

Immediately after the war Dr Schonland collected a small group of the brightest young men who had been associated with him in the field of radar and set them to work on the applications of radar to the study of atmospheric phenomena. He called this the Telecommunications Research Laboratory and set it up in the Department of Electrical Engineering of the University of the Witwatersrand.

One of the challenges presented to this laboratory was posed by Colonel Harry Baumann, then director of trigonometrical survey. He had been greatly impressed with the wartime developments in radar ranging and was convinced that there was tremendous scope for instruments which could measure distance with the accuracy required for geodetic and engineering survey purposes; but he recognized that a breakthrough in techniques was necessary because of the need for an increase in accuracy or about two orders of magnitude.

The response from the CSIR was typical. Although no success with such radio systems had been achieved elsewhere, I accepted the view of senior laboratory staff that there were no fundamental obstacles and authorized the work to proceed—even though the financial support being sought by Colonel Baumann had not yet been obtained. Such support never, in fact, materialized.

The work was entrusted to Dr Trevor Wadley, fresh from his remarkable success in the development of crystal controlled communication receivers. In a matter of months Wadley was able to demonstrate a working system with the accuracy necessary for geodetic purposes. This was the origin of the now well known Tellurometer system of distance measurement. With patents in the principal countries of the world, the CSIR was able to follow through with development and commercialization through the establishment of Tellurometer Ltd, in association with a Cape Town manufacturer, and establish a world-wide market for the Tellurometer system. Much of the credit for this must go to the initiative of Colonel J. H. Jeffrey, a Cape Town entrepreneur. Tellurometer Ltd was subsequently taken over by a more broadly based company, the Instrument Manufacturing Corporation, which, in turn, was taken over by Plessey. In the meantime, the laboratory's work on distance measurement has led to improvements in the Tellurometer system and recently to a new infrared system which is more suitable for close range work.

Underlying Principles

The case history of the Tellurometer is presented here in some detail (if somewhat sketchily) because it does illustrate a number of principles. (1) The project was included in the programme because there was an established need and a potential sponsor; (2) work was initiated because one of the staff was interested and was allowed to continue because the initial results showed promise; (3) technical and theoretical back-up in the research group contributed much to effective follow-through; (4) development and commercialization were successful because the CSIR was prepared to entrust it to an enterprising individual; (5) experience with the invention provided much of the "entrepreneurial know-how" of the South African Inventions Development Corporation—a statutory body—which was subsequently set up in close association with the CSIR to handle the patenting and development of inventions; (6) there were many occasions when crucial decisions had to be taken quickly and decisively and followed up by resolute action.

The Telecommunications Research Laboratory has since developed into the National Institute for Telecommunications Research, with its own building on the campus of the University of the Witwatersrand; the first director, Dr F. J. Hewitt, is now a vice-president of the CSIR. In spite of the name, its activities could be more accurately described as radio physics, for example radar measurement of rainfall and the application of radar to the study of lightning flash.

Some people may ask whether this research is not more appropriate to a university than to a national research institute. The CSIR has, however, an obligation to provide scientific services to meet the engineering requirements of industry and the technical agencies of government—in this case, for example, the South African Broadcasting Corporation, the General Post Office, the South African Airways and the armed services. This requires regular measurement, recording and interpretation of data connected with the environmental conditions affecting the propagation of radio waves and the provision of regular services to these agencies. This type of activity is obviously not appropriate to a university. But, at the same time, these phenomena are not completely understood and it is therefore essential that the service activity should have a broad base of fundamental research—subject to the condition that all projects should be relevant to the interests of actual or potential sponsors. Not only does this serve to attract and retain staff of suitable calibre but it also enables the national laboratory to provide a "window" to worldwide advances in the field.

Clearly the national laboratory will not be able to maintain this position if the standards of the services provided by the technical agencies concerned, and the manufacturing industry supplying equipment to these services, are not keeping pace with developments throughout the world. This requires scientists, engineers and technicians who are well grounded in the techniques involved, and who work against a background of current research. In this respect, the CSIR has a central role in the support of academic research. Its support of university research includes support for the research activities of academic staff—because research students will clearly not be attracted unless there are active research schools in the fields concerned.

In radio physics (or solar and terrestrial physics), for example, the CSIR supports ionospheric research and radio astronomy at Rhodes University, magnetospheric physics (micropulsations and whistlers) at the University of Natal, cosmic rays at Potchefstroom University — and, in the context of Antarctic research, it funds studies of geomagnetism through Potchefstroom University and of airglow through the University of Stellenbosch. The CSIR is also the national member of the International Council of Scientific Unions and thus of the International Union of Geodesy and Geophysics, the Union Radio Scientifique Internationale, the Committee on Space Research and the Scientific Committee on Antarctic Research. Such research (including that of the CSIR) is reviewed by the South African National Committee for Geomagnetism, Aeronomy and Space Sciences. This committee reviews South African participation in international programmes and activities initiated or coordinated at the international level by the International Council of Scientific Unions and provides a medium through which all who are interested in this field of science are kept in touch with each other.

A side-effect of this acceptance of responsibility in relation to global programmes was that, during the International Geophysical Year 1957–58, the CSIR undertook to operate optical and radio tracking stations for artificial Earth satellites on behalf of the United States national committee. Although South Africa had no part in these programmes, this was accepted as an international obligation because of South Africa's geographical position, which offered the first opportunity for interrogation of the satellites—twenty minutes after launching. Operation of the Minitrack (radio) Station by the National Institute for Telecommunications Research was so successful that the CSIR was later invited to operate a deep space instrumentation facility and a satellite tracking and data acquisition facility by NASA. The operation of these stations represents an enormous engineering exercise which is more appropriate to a national institute than to a university.

Sewage and Effluent

The National Institute for Telecommunications Research has been selected as an example to illustrate some aspects of the policies which have been evolved by the CSIR in fulfilment of the role and functions envisaged for it by its founder president, Sir Basil Schonland. Some other aspects may be brought out more clearly by considering the example of water research.

In the early days of the CSIR, the need for research into the treatment of sewage and factory effluent was brought to the attention of the CSIR by municipal chemists and their professional association, the Institute of Sewage Purification. At that time, two government agencies were concerned with water—the Department of Irrigation, which was traditionally concerned chiefly with water supply for agriculture, and the Department of Forestry, which had a well conceived programme of hydrological research into "forest influences". This was designed *inter alia* to provide data on the effects of afforestation on water supply. Thus the CSIR had to consider its position in relation to current research—or the lack of it—in hydrology and the foreseeable problems of water pollution. The last of these was a "horizon problem" —visible principally to the municipal chemists who were confronted with the problems that accompanied increasing industrialization and urbanization.

Confronted with this problem, which did not fit into any of the organizational patterns envisaged at that time, the CSIR decided on a tentative approach. It established a Water Treatment Research Unit in temporary accommodation at the University of the Witwatersrand and placed it under the direction of the National Chemical Research Laboratory. The decision to set it up in Johannesburg was coincidental to the extent that the chief city biochemist of Johannesburg, Mr H. M. Wilson, was at that time available, on retirement, to take charge of the unit. To lead the research, the CSIR recruited Dr G. J. Stander, the city biochemist of East London and a hot gospeller for the doctrine of water re-use as the only long term solution to the problem of water supply which would confront the country in the second half of the twentieth century.

The procedure adopted provides some interesting contrasts with that adopted in the case of radio physics. There was expertise available in radio physics, which was looking for applications in the transition from war to peace but, as far as water was concerned, there was just a "horizon problem", with no clear-cut lines of official responsibility for finding a solution. The CSIR therefore recruited the best available technological expertise within the framework of an institute under strictly academic and professional scientific direction.

The "tentative" approach of the CSIR paid off to the extent that, in response to the demand for the services of the Water Treatment Research Unit, it grew to the status of a division of the National Chemical Research Laboratory and, in 1957, to the National Institute for Water Research. Dr Stander is now the president of the International Association for Water Pollution and has left the CSIR to become deputy chairman and executive officer of a newly created statutory body, the Water Research Commission. And, for the record, the first municipal plant for the purification and recirculation of municipal sewage effluent in the world was commissioned at Windhoek in 1969 by the Prime Minister, Mr B. J. Vorster.

Methods of Organization

The two examples illustrate the principle that research cannot be organized from above. The policy of the CSIR has always been "to let the currency float"—in terms of current needs and available expertise and ability. At all times, staff have been required to prove their worth in terms both of the demand for their services from sponsors and of international recognition.

The principles deduced from these two examples illustrate most aspects of CSIR policy. For example, the National Physical Research Laboratory, which was established in 1946 and of which I was the first director, has provided the seed bed from which has grown the National Mechanical Engineering Research Institute, the National Research Institute for Mathematical Sciences and the National Electrical Engineering Research Institute. These research groups also provided the core from which was drawn the nucleus of staff of the Atomic Energy Board when the time was ripe for it to set up its own research establishment in 1959—under Dr A. J. A. Roux, formerly head of the Functional Efficiency Division of the National Building Research Institute, director of the National Mechanical Research Institute and vice-president of the CSIR.

Similarly, the National Chemical Research Laboratory was the nursery from which has grown the National Institute for Water Research, the National Nutrition Research Institute (recently split into the National Food Research Institute under the CSIR and the Nutritional Diseases Research Institute under the South African Medical Research Council), the Chemical Engineering Group, the Bantu Beer Research Unit, the Microbiology Research Unit (which has made particularly valuable contributions in the field of mycotoxins) and the Corrosion Research Unit.

Building Research

The third national research institute to be set up by the CSIR under Dr Schonland was the National Building Research Institute. The reasons advanced at the time for setting this up as a national institute and not as an industrial research association were that, in view of the horizontal organization of the building and construction industry, the prospects of gaining support for an adequate research effort in this field on an equal basis were unlikely. This virtually enunciated a principle which has since become part of CSIR policy towards industrial research, namely that in industrial sectors where a need for research has been identified, it is incumbent on the CSIR to initiate research under the umbrella of an existing institute and to build it up with industrial support.

In 1945 and 1946, the most urgent need was for low cost, high density urban housing for the Bantu population. Wartime conditions had resulted in the crowding of the rural population into the cities and, with the prospect of burgeoning industrial development, there was every indication that the problem would become more acute.

Under Mr E. W. Dohse, chief engineer of the Department of Public Works, who was seconded to direct this institute, the problem was solved by a comprehensive programme involving all sections of the community. The principles of design and construction which were evolved have since been applied by many developing countries in Africa, South East Asia and South America. The institute has subsequently moved on to make important contributions to community services such as the design of schools, hospitals and homes for the aged and to specific problems such as the erection of buildings on expanding clay foundations and the utilization of blast-furnace slag with a high magnesia content for the production of slag cement.

The chief contribution of this institute, however, may well have been in the establishment of a Building Research Advisory Committee, which has brought together leading representatives of all sections of the building and construction industries. Quarterly meetings of this committee have provided a neutral forum for the discussion of technical issues affecting all sections of the professions, industries and trades between which there was previously no constructive dialogue. This institute has provided the home for the development of a Timber Research Unit and a Ceramics Research Unit—on the grounds that the principal industrial support was forthcoming for the use of these products in the building and construction industries.

In the field of housing, the CSIR became involved with human problems. But it had to face up to these from the start because of its obligation to "explore and develop the whole field of medical research" and by a special request to advise on the future of the Aptitude Tests Section of the wartime South African Air Force. This service, under Dr Simon Biesheuvel, had achieved great distinction during the war in the classification and selection of aircrew personnel. The CSIR decided, at its first meeting, to provide a "home" for its records, through the creation of a National Bureau for Personnel Research. Within the framework of the CSIR's policy for contract research, this soon developed into the National Institute for Personnel Research under Dr Biesheuvel's direction, which made its mark in the development of procedures for the selection, classification and training of workers—first in the mining industry but later in other fields of commerce and industry. This unique development is, to some extent, a reflexion of the CSIR's policy of allowing research to find its own level in response to demand for research services, the need for these particular services in a situation of rapid industrial development in a largely rural community (to a great extent primitive and tribal) and the particular abilities of the research leader. With the establishment of a separate Human Sciences Research Council, the future control of this research is under review, but there is no doubt that those aspects which are directly concerned with personnel management are inseparable from industrial research.

Fatty Acids and Hydrocarbons in Surtsey Sediment

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Hydrocarbons and fatty acids were examined from the sediments of a marine lagoon on Surtsey, an island formed by a volcanic eruption in 1963. The distribution of both hydrocarbons and fatty acids indicated that correlations can be made between the primary organisms observed in the lagoon, Chlorophycophyta, and the sediment components identified.

In 1963, a submarine eruption began approximately 20 miles off the south coast of Iceland, which gave rise to the island Surtsey. There was a gradual decrease in volcanic activity in 1964 and 1965, ceasing entirely at the end of April 1965. In the spring of 1964 the first biological observations were made. Since that time, colonization of plants and animals has been routinely surveyed. Growth conditions for newly arriving plant parts have been poor because the substrate is composed primarily of lava, tephra or secondary beach substrata[1]. Of two lagoons formed, the older, which formed on the northern side of Surtsey, was studied in detail. In May 1965, filamentous Chlorophyceae were observed on the shore east of the lagoon and by 1967 the lagoon was populated by gulls. Large faecal deposits led to heavy microbial development. Just beneath the water's edge, brown layers developed in which large numbers of unicellular chlorophycean algae and rare flagellates[2] could be seen. The lagoon gradually dried up and by June 1970 only a brown-caked basin remained[3]. The sample used in this analysis was collected from the upper 6 cm of the surface of the dry lagoon and stored in a polyethylene bag. The sediment was a fine-grained, green mud with no apparent mat formation.

Biological compounds and their degradation products are found in trace amounts in sediments. It has been shown that a direct correlation can be made between lipids originating from biological sources and those found in geological sources[4,5]. Although each new species of bacteria, plant, and animal has been carefully recorded by biologists, no organic geochemical studies have been made on sediments. The only exception to this was the organic geochemical investigation of the amino-acids and hydrocarbons from the freshly fallen ash from an eruption resulting in the formation of the island, Syrtlinger, which occurred less than 1 mile from Surtsey. Ponnamperuma[6] has reported the presence of alanine and aspartic acid, and traces of glycine and serine at a total concentration of only 10 p.p.b. in the freshly fallen ash of Syrtlinger; no hydrocarbons were detected. Further studies of the ash amino-acids have been carried out by Fridriksson[7]. The island of Surtsey presents a unique source for organic geochemical study[8] because the organisms which contribute to the Surtsey sediments are known.

The sample was treated with dilute hydrochloric acid to remove carbonate and washed with distilled water to remove soluble inorganic salts. After filtration, the sample was subjected to four successive 30 min chloroform extractions with ultrasonic vibrations. The sample was filtered after each extraction and the extract taken to dryness on a rotary evaporator. The lipid residue was weighed and then saponified using 0.5 N potassium hydroxide in methanol for 2 h with gentle refluxing. The nonsaponifiable fraction, containing the hydrocarbons, was separated from the saponifiable fatty acid fraction by extraction of the alkaline solution with benzene. The separated nonsaponifiable fraction was then dried under a stream of dry nitrogen and taken up in 1 ml. of hexane. This was placed on a chromatographic column packed with prewashed silica gel and silicic acid (1:1, v/v) (Woelm, activity 1). The aliphatic hydrocarbons were eluted with 100 ml. of hexane and the hexane fraction dried on a rotary evaporator at 60° C. This hydrocarbon fraction was weighed and used for identification by means of gas-liquid chromatography. The saponifiable alkaline fraction was acidified with hydrochloric acid to *p*H 3 and extracted with benzene. The fatty acid–benzene fraction was taken to dryness. Methylation of the free fatty acids was accomplished by using BF_3–MeOH reagent. The fatty acid methyl ester fraction was weighed and used for identification by means of gas-liquid chromatography. The filtered sediment was then treated with 0.5 N potassium hydroxide in methanol and subjected to ultrasonic vibrations for 30 min. The sample was filtered and the alkaline solution was extracted with benzene. This benzene fraction was taken to dryness,

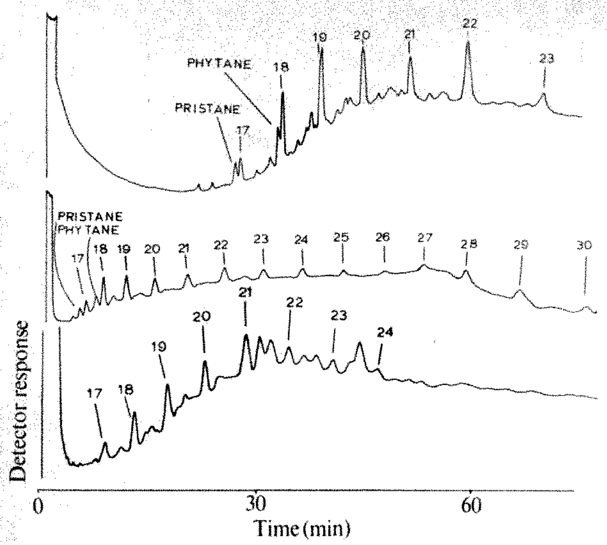

Fig. 1 Gas chromatogram of alkanes from Surtsey sediment (from lipid extracts). Top, stainless steel capillary column (150 feet × 0.02 inches internal diameter) coated with Apiezon L. Barber Colman (series 5000) gas chromatograph with helium flow of 9 ml./min (using split). Temperature programmed from 150° C to 230° C at 3° C/min. Middle, copper column (8 feet × 1/8 inches outer diameter) packed with 5% FFAP on Varaport 30. Barber Colman (series 5000) gas chromatograph with helium flow of 30 ml./min. Temperature programmed from 150° C to 225° C at 3° C/min. Bottom, gas chromatogram of alkanes from Surtsey sediment (from KOH-MeOH extraction). Barber Colman (series 5000) gas chromatograph with helium flow of 35 ml./min. Temperature programmed from 150° C to 230° C at 3° C/min.

weighed, and the hydrocarbons fractionated by silica gel/silicic acid column chromatography. The hydrocarbons were identified primarily by gas-liquid chromatography.

Table 1 Analytical Analysis of Surtsey Island Sediments

Dry weight sediment	1,419.2 g
Lipid extract dry weight	0.0192 g
Hydrocarbon dry weight	0.0036 g
Fatty acid methyl esters dry weight	0.0094 g
Exhaustive KOH-MeOH extract hydrocarbon dry weight	0.0009 g
Largest hydrocarbon component	C22 : 0
Largest fatty acid component	C18 : 1
$\frac{\text{Percentage lipid}}{\text{Sediment weight}}$	0.0013%
$\frac{\text{Percentage hydrocarbon}}{\text{Sediment weight}}$	0.00025%
$\frac{\text{Percentage fatty acid ester}}{\text{Sediment weight}}$	0.00066%
$\frac{\text{Percentage hydrocarbon}}{\text{Lipid weight}}$	18.75%
$\frac{\text{Percentage fatty acid ester}}{\text{Lipid weight}}$	48.95%

A gas chromatograph (Barber Colman, series 5000) with flame ionization detectors, operated using temperature programming, was used for identification. Retention times in gas-liquid chromatography are not unique, so we verified the identifications by using two different columns, Apiezon L and FFAP (Varian), a non-polar and polar substrate respectively. Stainless steel, wall-coated open tubular columns, 150 feet × 0.02 inches (internal diameter), and copper columns, 8 feet × 1/8 inches (internal diameter), were used for separations. Analytical results are shown in Tables 1 and 2. Fig. 1 contains chromatograms showing total hydrocarbon fractions. The hydrocarbons obtained from saponification were injected onto a 6 foot 1% SE-30 column of an LKB-9000 gas chromatograph-mass spectrometer and programmed from 130°–260° at 5° C/min. The mass spectra were scanned with a total ionizing current of 20.0 eV.

Table 2 Percentage Composition of Hydrocarbon Components from Chloroform Extracts

Hydrocarbons	Percentage composition
n-16	Trace
Pristane	4.2
n-17	7.0
Phytane	7.6
n-18	14.0
n-19	15.3
n-20	9.5
n-21	6.4
n-22	7.7
n-23	4.9
n-24	6.2
n-25	2.3
n-26	2.3
n-27	4.1
n-28	2.1
n-29	3.0
n-30	1.9
n-31	1.5

Fig. 2*A* shows the mass spectrum of the first component, which has a molecular ion at *m*/*e* 240, corresponding to normal C_{17}, and prominent fragment ions at *m*/*e* 113, 183 and 253 corresponding to pristane. Fig. 2*B* shows the mass spectrum of normal C_{19} saturated hydrocarbon. The slight enhancement of the ion at *m*/*e* 225 may indicate some contribution of the *iso* C_{19} alkane, 18-methylnonadecane. Fig. 2*C* gives a mass spectrum indicative of a mixture containing C_{21} hydrocarbons with one and two degrees of unsaturation.

Table 3 Percentage Composition of Fatty Acid Esters

Fatty acid ester	Percentage composition
12 : 0	1.45
14 : 0	10.51
16 : 0	28.09
16 : 1	7.26
18 : 0	18.16
18 : 1	37.88
Others	1.21

Other mass spectra indicate that the hydrocarbons of the sediment may be far more complex than the gas chromatogram indicates. There are indications of additional straight-chain hydrocarbons ranging from C_{23}–C_{36} with zero to three degrees of unsaturation. There were also traces of what may correspond to C_{25}–C_{27} aromatic hydrocarbons. No measurable hydrocarbons or fatty acids were found in the procedure using controls and solvent blanks.

Hydrocarbons are present in recent sediments, usually in concentrations of parts per million (p.p.m.) and seldom exceeding one part per thousand (p.p.t.). The Surtsey sediment amsple contained a hydrocarbon concentration of approximately 2 p.p.m., the low value due to low productivity of the island. Straight-chain hydrocarbons ranging from C_{17} to C_{25} were present in the Surtsey sediment, C_{22} being the largest normal hydrocarbon component. Pristane (2,6,10,14-tetramethylpentadecane) and phytane (2,6,10,14-tetramethylhexadecane), isoprenoid hydrocarbons, which probably arise from diagenetic degradation of algal chlorophylls, were present in trace amounts. But these isoprenoids do occur in some species of benthic algae[9] and in some bacteria[10,11]. Whereas higher plant alkanes show a marked trend towards odd-numbered carbon atoms between C_{25} and C_{33}, the Surtsey sediment alkanes show no marked odd/even tendency, as would be expected from a sediment which had no contributions from higher plants.

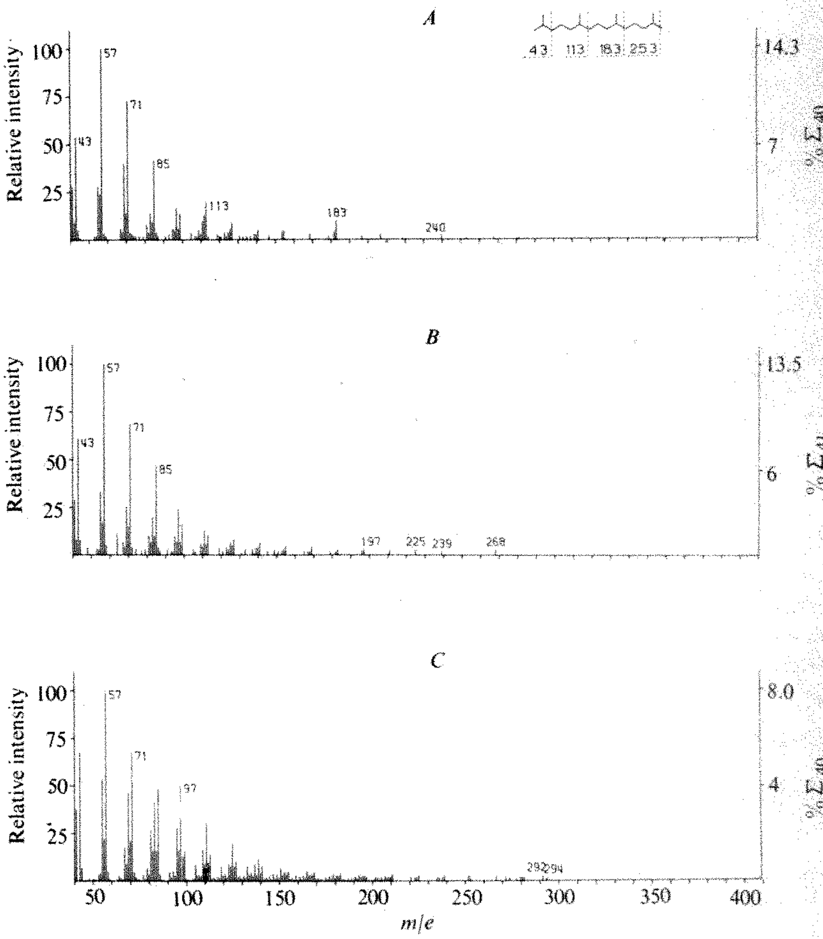

Fig. 2 *A*, Mass spectrum of pristane and normal C_{17} hydrocarbon; *B*, mass spectrum of normal C_{19} hydrocarbon; *C*, mass spectrum of mono and diunsaturated C_{21} hydrocarbon.

If blue–green algae were the principal invader of the lagoon studied, one would expect to find a precursor relationship between the hydrocarbons found in blue–green algae and the hydrocarbons found in the sediment. This was not observed. Some bacteria, however, exhibit hydrocarbon distributions similar to that found in the Surtsey sediment[10,15]. Chlorophycophycean algae (green algae) exhibit a more complex hydrocarbon distribution than Cyanophycophycea (blue–green algae). Hydrocarbons from several species of *Chlorella*[16] grown autotrophically under fluorescent light contained a series of saturated n-paraffins ranging from 17 to 36 carbon atoms in length. Among the algae found on Surtsey, Chlorophycophyta was the group most frequently found[2] and the hydrocarbons found in the sediment contained corresponding carbon chain lengths.

The hydrocarbons extracted from the sediment with chloroform and those from the exhaustive KOH-MeOH extraction were qualitatively the same in the lower molecular weight range (Fig. 1). But there were large, unidentified peaks in the C_{21}–C_{24} molecular weight region in the chromatogram of the KOH-MeOH extracted hydrocarbons, which were absent in the chloroform extracted hydrocarbon fraction as shown (see Fig. 1). Also the higher molecular weight hydrocarbons (C_{25}–C_{30}) were absent in the KOH-MeOH extracted sample. As noted, the chromatograms of the exhaustive KOH-MeOH and the chloroform extracted hydrocarbons were not identical. This indicates that there is complex organic matter not extractable by lipid solvents alone.

Fatty acids are major lipid components of all living organisms which normally show a predominance of even-carbon numbered fatty acids. Algae contain a narrow range of fatty acids generally ranging from C14 : 0 to C18 : 4 (refs. 5, 17, 18, 19). Polyunsaturated fatty acids are absent in bacterial lipids; the mono-unsaturated acid, 11-*cis*-octadecenoic acid, is the largest component in photosynthetic bacteria. In contrast, 9-*cis*-octadecenoic acid is the major monoenoic acid found in blue–green algae. In general, blue–greens usually have 16 : 0 or 16 : 1 as their major fatty acid components while green algae have an unsaturated C_{18} as their major fatty acid[17]. The fatty acids (both free and bound) from the Surtsey sediment consisted of three major components, a straight-chain C14 : 0, a straight-chain C16 : 0, and a straight-chain C18 : 1 fatty acid (Table 3). Other minor components identified by their retention times were C12 : 0, C16 : 1, and C18 : 2 fatty acids. Further characterization of the C_{18} monoenoic acid found in the Surtsey sediment might further define the course of this acid.

Knowing the distributions and concentrations of both acids and hydrocarbons from the Surtsey sediment, however, it seems that green algae were the primary contributors of organic matter to the lagoon during its short existence, although bacteria may have made some contribution. Blue–green algae are considered to be one of the more primitive organisms and the fact that this lagoon was observed to be inhabited primarily by green algae during the few years of its existence is of interest as well as the fact that the record of their brief inhabitance has been chemically preserved in the lagoon sediment.

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Cen XR-3 : A Neutron Star Younger than the Crab ?

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A model for the pulsed X-ray source Cen XR-3 has been constructed, based on studies of wobbling, young, evolving neutron stars which are generating heat in their crusts by the conversion of rotational energy through precession-induced cyclic strain. The observational features can be understood if the observed period is interpreted as the free nutation period. We predict the actual rotational period to be ~8 ms and the slow-down rate $\sim 8\times10^{-13}$ s s^{1}.

REMARKABLE variations in the X-ray flux from Cen XR–3 have been reported by Giacconi *et al.*[1]. These have the following characteristics: (1) There is an observed periodicity at ~4.87 s with a large duty cycle, the available data cannot exclude the presence of additional periods shorter than ~0.096 s; (2) the intensity was observed to increase ("flare") by a factor of 10 in about 1 h, and in the same 24 h interval the period was seen first to decrease and then to increase suddenly by 0.02% and 0.04%, respectively, each change occurring in $\sim 10^3$ s; (3) the observed period has shown a secular decrease of ~0.6% in a 3 month interval; (4) the "flare" X-ray spectrum observed in April 1971 can be fitted with a black-body curve corresponding to a temperature $\sim 3.3\times10^7$ K (or a thermal bremsstrahlung law with kT ~16 keV and an exponential cut-off at ~4 keV).

Wobbling Neutron Star Model

We wish to show in this article how most of these striking properties can be understood in the light of a recent study of wobbling, young, evolving neutron stars[2,3] and in terms of our recently developed theory of heating in these objects[16]. This theory contends that rotational energy can be converted into heat in neutron-star crust by the action of precession-induced cyclic strain in the crystalline mantle and/or by core-mantle coupling (although this is expected to be less important)[4]. We have already considered Cen XR–3 as a possible application of this theory of neutron-star heating, and we have accordingly predicted its rotation period to be $\lesssim 10$ ms. We show here that this prediction can be reconciled with the new observations by supposing that the period which has been observed by the ASE group[1] corresponds to the free nutation period of a triaxial neutron star.

It is perhaps not immediately obvious how such a periodicity might show itself in pulsed black-body emission. We therefore refer to the configuration of Fig. 1 where we have presented a simplified picture of the rigid body motion. The total angular velocity is shown as the vector ω, fixed in space to a high degree of approximation. It is taken to be at an angle θ with respect to the 3 axis, the axis of maximum moment of inertia. The observer's line of sight makes an angle i with the rotation axis so that the great circle $\overline{OH}$ represents the observer's horizon on the neutron star's surface. The axis m represents the radius vector to an assumed hot spot, which is likely to lie on the magnetic axis. The intersections of the dashed planes (passing through the hot spot perpendicularly to ω) with the stellar surface are the effective emission bands seen by an observer who cannot time-resolve on the scale of $2\pi/\omega$. As the axis m nutates ($\theta = \theta(t)$) from position 1 to position 2 through even a small angle ($\sim \delta\alpha/(H_e + \delta) \ll 1$ where $\alpha = \theta_{\max}$, $H_e \equiv H_{1e}$ is the effective dynamical ellipticity and $\delta = H_{2e} - H_{1e}$ is a measure of the triaxiality[3] in the case where the 3 axis is taken to be the dominant mass axis), the arc of the emission band that is visible to the observer can change markedly as indicated by the different intersections $\overline{E_1M_1}$, $\overline{E_2M_2}$. It may be shown that the eclipsed arc S is given by $\tan S/2 = \tan(\chi + \theta) \tan i$, and hence that $dS/d\theta = 2 \tan i/(\cos^2(\chi + \theta) + \sin^2(\chi + \theta) \tan^2 i)$. Thus when $\chi + \theta_{\min} \simeq \pi/2$ the fractional change in the observed arc length over a nutation period is, for small angles, $\Delta S/S \sim (\delta/(H_e + \delta))\, \alpha/i$. For the nutation to be effective in modulating the X-ray emission, this should be roughly equal to the observed depth of modulation in the X-ray flux $\Delta F_x/F_x \sim 0.7$. Thus it is clear that we require $i \sim (\delta/H_e + \delta)\,)\alpha$ and our line of sight to Cen XR–3 must be closely aligned with its rotation axis. We would not then expect to see a radio pulsar, because the radio beaming is generally thought to originate at a large angle with ω, near the magnetic axis. We also note the possibility of $\theta_{\min} \rightarrow \sim -\chi$, $+\theta_{\min} \simeq 0$. This is the aligned-oblique rotator configuration with ω precessing on the body cone containing m[5] and $\chi \gtrsim 55°$. Here we find $\Delta S/S \sim (\delta/(H_e + \delta))\, \alpha/(\pi/2 - i)$ so that the line of sight would have to be nearly perpendicular to ω, and we would expect at least the normal chance of observing a radio pulsar. In this case, however, the neutron star crust must be an almost perfect Coulomb crystal in order to support the strain of such a large wobble amplitude without exceeding its elastic limit and flowing plastically to a new equilibrium configuration. Although possible, this model seems rather unlikely, so we shall not consider it further at this time. It is clear that the angular extent of the spot (thickness of the emission band) would have to be $\lesssim (\delta/(H_e + \delta))\, \alpha$ with a high duty cycle more likely when the equality holds. Of course this mechanism will not work if there are two equally intense hot spots on either end of a diameter (for example, a magnetic axis). The reason is that as one band is eclipsed the other emerges. But although we expect hot spots to form near magnetic poles, there is no reason to suppose that the field is symmetric about a plane passing through the centre of the star. An axially displaced dipole model has been used to explain the observed asymmetric properties of several magnetic stars[6–8]. Such a model would have important implications for the formation of hot spots. If the displacement of the magnetic dipole along its symmetry axis is by a distance a_R (in units of the stellar radius R), then the ratio of the polar fields is $B+/B- = (1 + a_R)^3/(1 - a_R)^3$. Hence, the effective thermal conductivity along the field might be enhanced (over the conductivity normal to the field) by an additional factor of $(1 + a_R)^6/(1 - a_R)^6$ at the + pole relative to the – pole. Moreover, one can show that the angle subtended at the centre of the star by the + polar region (that is, the region where field lines pass outwardly through the stellar surface) is given by ($a_R^2 \neq 0$) $\sin^2\varphi = (2/a_R^2)\,[-(1 + a_R^4) + (1 + a_R^2)\sqrt{a_R^4 - a_R^2 + 1}]$. In three magnetic stars, a_R has been found to range from ~ 0.1 to ~ 0.6[6–8] yielding φ in the range $\sim 81°$ to $\sim 36°$. Here we shall require $\varphi \lesssim \alpha\delta/(H_e + \delta)$ which leads to rather larger values of a_R (for example, $a_R \sim 0.93$ for $\varphi \sim 10^{-1}$ radians, $a_R \sim 0.99$ for $\varphi \sim 10^{-2}$ radians). This would place the effective sources of the field at, or just outside, the core-mantle boundary in typical neutron stars, which might be the result of flux exclusion from a super-conducting core, or the loss of the outer layers of a main sequence magnetic star in the course of its evolution into a neutron star.

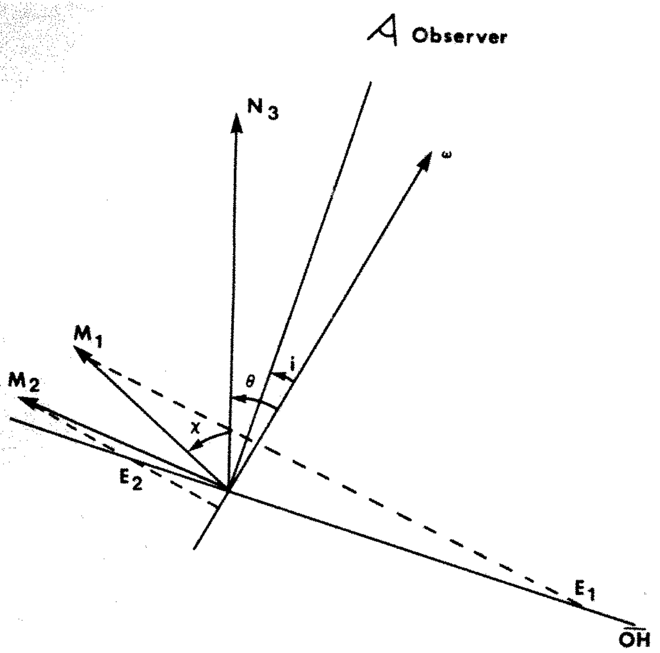

Fig. 1 ω is the total angular velocity vector making an angle i with the line of sight. $\overline{OH}$ is the diameter of the great circle representing the observer's horizon on the neutron star. M_1 and M_2 are the radius vectors to the single hot spot on the surface at two different times and E_1M_1, E_2M_2 represent the corresponding visible emission bands.

The Nutation Period

The free nutation period can be written in the limit of small angles[9] as

$$P_N \simeq P/2\sqrt{H_e(H_e + \delta)} \qquad (1)$$

where P is the spin period about the 3 axis. We shall set $\delta \sim H_e$ (see below) and take H_e as the remanent ellipticity[5] given by $H_e \simeq 1.4 \times 10^{-12}\ \mu_{30}\ a_6^7\ M^{-3}\ (2\pi)^2\ P^{-2}$ where μ_{30} is the (uniform) rigidity of the crust in units of 10^{30} dynes cm^{-2}, a_6 is the "effective" radius of the crust in units of 10^6 cm and M is the mass of the star in units of the solar mass. If we now identify P_N with the observed X-ray periodicity of ~ 4.87 s, and if we set $a_6 \sim 1.2$, then we find from equation (1) that

$$P \simeq 1.4\ \mu_{30}^{1/3}\ M^{-1}\ \text{ms} \qquad (2)$$

The expected equivalent black-body temperature can be written as

$$T_s \simeq 3.24 \times 10^9\ (4\pi\, g/\Omega_s)^{1/4}\ (M\ \xi^2\ P^{-3}\ \mathring{P})^{1/4} \langle\theta^2\rangle^{1/4}\ \text{K} \qquad (3)$$

Here, ξ is the radius of gyration in units of the stellar radius; the time average is over a nutation period so that $\langle\theta^2\rangle \simeq$

θ^2_{max} $(1-\delta/2(H_e+\delta))=\alpha^2$ $(1-\delta/2(H_e+\delta))$; Ω_s is the solid angle of the hot spot; and g is a gyroscopic factor that is $\simeq\frac{1}{2}$ for $\chi\simeq\pi/2$. But this expression for T_s has been written assuming that the entire amount of heat generated in the crust would emerge from the spot. This is unlikely to be the case and, in general, we might expect only a fraction $\Omega_c/4\pi$ of the heat generated to be channelled (for example, by the magnetic field) through the hot spot, where Ω_c is then the effective collection solid angle for the spot. One model of the field that achieves this situation is provided by a point dipole situated in the crust. We assume that the core excludes the field lines so that there is an image dipole interior to the core-mantle boundary. The region of magnetic field in the crust enclosed by the same limiting field line as was discussed above is effectively flattened and extended as a result and may be thought of as yielding the collection solid angle Ω_c. Thus the 4π in the equation for T_s should be replaced by Ω_c.

It can be seen also that

$$\Omega_s\ T_s{}^4 \lesssim \Omega_c\ T_b{}^4 \tag{4}$$

where T_b is the mean temperature of the stellar surface outside the spot $(4\pi-\Omega_c)$. This result constrains the background flux to be greater, by a factor $\sim(2\pi-\Omega_c)/\Omega_c$, than the spot flux. We must therefore take care to arrange that T_b is considerably smaller than T_s so that modulation of the soft X-ray flux occurs as the spot visibility changes.

From these arguments for effective modulation, we expect $\Omega_s\simeq\pi\alpha^2\,(\delta/(H_e+\delta))^2$. The appropriate value to choose for T_s in formula (3) is the equilibrium or quiescent value. Unfortunately it is not clear what this value is, as the most recent measurement[1] is appropriate to post-flare conditions. An earlier determination by the Leicester group[10] gave a black-body temperature of $\sim2.3\times10^7$ K. However, the spectrum at the high-energy end was not determined from simultaneous observations, and from the photon count it would seem that flaring was also present during this observation. Perhaps the best procedure at this juncture is to combine the observed factor 10 increase in photon flux in the 2–6 keV band with the observed flare temperature ($\sim3.3\times10^7$ K) to deduce a pre-flare value. This leads to $T_s\sim1.5\times10^7$ K.

We proceed now by using equation (2) with equation (3) to find

$$\mathring{P}\simeq0.5\times10^{-18}\ \mu_{30}\ M^{-4}\ \Omega_c{}^{-1}\ \xi^{-2}\ T^4_{s7} \tag{5}$$

where T_{s7} is the quiescent spot temperature in units of 10^7 K (~1.5). From equation (4) the corresponding expression for T_{b7} becomes

$$T_{b7}\ \simeq\ \alpha^{\frac{1}{2}}\ \Omega_c{}^{\frac{1}{4}}\ T_{s7} \tag{6}$$

It is likely that $\mu_{30}\lesssim1$, $M\gtrsim0.1$ and $\xi^2\gtrsim0.01$, so we have the limits, $P\lesssim14$ ms, $\mathring{P}\lesssim5\times10^{-13}\ T^4_7\ \Omega_c{}^{-1}$ s s^{-1}. We shall attempt to sharpen the estimates below when we discuss the secular behaviour.

Distance to Cen XR-3

We may with this model immediately estimate the distance, D, to Cen XR–3 from $2\pi D^2\ F_m\simeq9.0\times10^{31}\ T^3_{s7}\ \Omega_s R^2$, where F_m is the observed X-ray energy flux in unit bandwidth at maximum (in keV/keV cm^2 s) and T_{s7} is the spot temperature in units of 10^7 K. Thus, on using the previous estimate for Ω_s, we find

$$D\ \simeq\ T_{s7}{}^{3/2}\ \alpha\ R_6\ F_m{}^{-\frac{1}{2}}\ \text{kpc} \tag{7}$$

With $T_{s7}\simeq3.3$ and $F_m\simeq1.0$ keV/keV cm^2 s as observed[1] (post-flare), this becomes

$$D\ \simeq\ 6\ \alpha\ R_6\ \text{kpc} \tag{8}$$

Our detailed calculations suggest that X-ray flaring and spin changes of both signs are expected if our model applies to objects like Cen XR–3. Fluctuations (as opposed to the regular nutation) in the wobble amplitude can be induced by relaxation of the wobble through plastic distortion and subsequent re-excitation through core-mantle coupling, when the maximum wobble angle α is near the elastic limit $\alpha_L\sim2\varphi_m/H_f$ (φ_m is the maximum angle of elastic shear and H_f is the fluid part of the ellipticity). These wobble changes release heat energy ΔW given by $\Delta W\simeq1.4\times10^{33}\omega^4\mu_{30}a^9_6\ M^{-2}\ \Delta(\alpha^2)$ erg. For Cen XR–3 (equation (2)) this becomes $\Delta W\simeq3\times10^{48}\ M$ $\mu_{30}^{-1/3}\ \Delta(\alpha^2)$ erg, which over a thermal diffusion time τ_D produces a mean "flaring" flux

$$\Delta W/\tau_D\ \simeq\ 3\times10^{48}\ M^2\ \mu_{30}^{-1/3}\ \tau_D{}^{-1}\ \Delta(a^2) \tag{9}$$

Taking $\tau_D\ \sim10^5$ s (the post-flare flux was observed to be approximately constant for at least 1 day), and taking $\Delta(\alpha^2)$ $\sim10^{-5}$ ($\lesssim\alpha_L^2$), $\mu_{30}\ \lesssim1$, and $M\gtrsim0.1$, we find $\Delta W/\tau_D\gtrsim3\times10^{36}$ erg s^{-1}. From equation (8) we find $D\sim0.6$ kpc, with $\alpha\sim\alpha_L$ $\sim10^{-2}$ and $R_6\sim10$ corresponding to $M\sim0.1$, for which the flare flux required[1] is $\simeq10^{36}$ erg s^{-1}. Thus the energy requirement can be met by the wobble changes even in this most stringent minimum mass limit. (This model is refined below.)

Spin Changes

The associated spin changes, however, are for the present case only of order $\Delta P/P\sim5.3\times10^{-9}\ M^{-2}\ \mu_{30}^{2/3}\ \Delta(\alpha^2)$, or $\lesssim5.3\times10^{-7}\ \Delta(\alpha^2)$. As the observed values are ~2–4×10^{-4}, this last result clearly does not suffice. But this may be the same circumstance that arises in the Crab[11] and Vela objects (reported at URSI meeting, April 1970), where there is a range of spin changes from values of order $\Delta P/P$ given above to the much larger starquakes ($\Delta P/P\sim10^{-9}$ for Crab, $\sim10^{-6}$ for Vela). The latter events seem to be quite different phenomena.

The starquake model of the large spinups[12] envisages relaxation in the figure of the star due to "cracking" of the crust. Recently we suggested[3] that alternately stressing and relaxing the internal magnetic field can have similar results. This seems capable of explaining both the unusual secular behaviour and the spin changes of Cen XR–3. It follows from equation (1) that

$$\Delta P_N/P_N=\Delta P/P\ [2+1/(1+\delta/H_e)]-(\Delta\delta/2\delta)\ \delta/(H_e+\delta) \tag{10}$$

where we have used $H_e\propto P^{-2}$. If $\Delta P/P$ is small, and taking again $\delta\sim H_e$, this becomes approximately $\Delta P_N/P_N\sim-\Delta\delta/4H_e$. If we identify this fractional change in P_N with the observed value of 4×10^{-4} (this occurs over $\sim10^3$ s, but even if the net change is the sum of numerous smaller ones our arguments apply) then $|\Delta\delta|\ \lesssim\ 1.6\times10^{-3}\ H_e$. With $H_e\ \sim0.94\times10^{-4}$ $M^{-1}\ \mu_{30}^{1/3}$ for Cen XR–3, this is $|\Delta\delta|\ \lesssim\ 1.5\times10^{-7}\ M^{-1}\ \mu_{30}^{1/2}$. This can be smaller than δ_m[13] (δ_m is the magnetic contribution to δ; $\sim10^{-8}$ for a mean internal field of 10^{13} Gauss and $\sim10^{-4}$ for a mean internal field of 10^{15} Gauss in a star of $\sim0.1\ M_\odot$) as it must be for the suggestion to be tenable ($|\Delta\delta/\delta|$ $\lesssim\delta_m/\delta$). Thus the magnitude of the spin changes is explicable in terms of fluctuations in the internal magnetic field. We must interpret the spindowns ($\Delta\delta<0$) in terms of "relaxations" in the stressed field[3]. The spinups ($\Delta\delta>0$) are less naturally explained on this model, but possibly they can be understood in terms of irregular yielding (cracking) of the crust. For it is the adjustment of the figure of the star to the new equilibrium figure which we suppose to stress the field and amplify it (see below). If this proceeds irregularly, sudden amplifications can occur. Such sudden yielding is likely to be associated with intervals of plastic deformation and heating, near the elastic limit. We note that in a spindown ($\Delta\delta_m<0$ and also $\Delta\ \mathcal{M}\ <0$ where $\mathcal{M}$ is the magnetic energy of the star) the magnetic energy dissipated (presumably in some resistive instability which we cannot hope to specify at this time) is also available for heating. In fact $\mathcal{M} \sim 5/3 \times 10^{43}\ a_6^3\ \overline{B}_{13}^2$ ($\overline{B}_{13}$ is the volume-weighted mean field in units of 10^{13} G), and a comparison with equation (9) shows that such heating could be dominant if a significant fraction of $\mathcal{M}$ is, in fact, dissipated. The spin-down event would then bear a remarkable resemblance to a solar flare.

Secular Behaviour

For secular changes in P_N, equation (10) may be written as

$$\mathring{P}_N/P_N = (\mathring{P}/P)\,(2+1/(1+\delta/H_e)\,) - (\mathring{\delta}/\delta)(\delta/(H_e+\delta)\,) \qquad (11)$$

We also write

$$\delta = \delta_m + \delta_f$$

where δ_f is a triaxiality that was established when the crust first formed (presumably on the Jacobi sequence)[14,15]. We might expect δ_f to be secularly dependent in the same way as H_e ($\propto P^{-2}$) and that $\delta_f \simeq H_e$ (quite possible on the Jacobi sequence). In this way δ can be $\sim H_e$ in accordance with our earlier assumption, even if $\delta_m \ll H_e$.

We shall find below that $\mathring{\delta}_m > \mathring{H}_e$ which is $\sim \mathring{\delta}_f$ so that $\mathring{\delta} \sim \mathring{\delta}_m$. Moreover, as $\delta_m \sim \mathcal{M}/-\Omega$, where Ω is the gravitational energy of the star, we have $\mathring{\delta}_m/\delta_m \simeq \mathring{\mathcal{M}}/\mathcal{M}$, since the term in $\mathring{\Omega}$ is down in magnitude by a factor $\mathcal{M}/-\Omega$. As the star adjusts its geometry in the course of the secular slowdown, we expect the field to become stretched and thus amplified at a rate corresponding to the secular release of gravitational energy. Thus we estimate $\mathring{\mathcal{M}} \sim -\mathring{\Omega}$. But it has also been shown[3] that $\mathring{\Omega} \simeq (5/8)$ $(\omega^2/\pi G\rho)\ \mathring{E}\ (\omega^2/\pi G\rho \ll 1)$, where ρ is the mean density and $\mathring{E}$ is the rate for change of rotational energy. Thus we can write $\mathring{\delta}_m/\delta_m \simeq -(5/8)\ (\omega^2/\pi G\rho)\ (E/\mathcal{M})\ (\mathring{E}/E)$, and hence from equation (11) we have

$$\mathring{P}_N/P_N = (\mathring{P}/P)\ [2+1/(1+\delta/H_e) - (5/4)\ (\delta_m/(H_e+\delta)\,)\ (\omega^2/\pi G\rho)\ (E/\mathcal{M})] \qquad (12)$$

Clearly either a secular decrease or increase in P_N is predicted, depending on whether or not the second term in the bracket dominates. This term is $\simeq H_e^{-1}\,(E/(-\Omega)\,)^2$, or $\sim 5 \times 10^2 M^3\, \mu_{30}^{-2}$ numerically. This must be large compared with $(2+1/(1+\delta/H_e)\,) \simeq 2.5$ for the observed secular decrease to be explicable in terms of the nutation period. In view of the uncertainties in our various calculations, we are of the opinion that this number should be at least ~ 10. Thus we require

$$M\ \mu_{30}^{-2/3} \gtrsim 0.27 \qquad (13)$$

although a smaller limit by up to a factor ~ 1.5 is possible. Thus we can obtain from equation (2)

$$P \lesssim 5.2\ \mu_{30}^{-1/3}\ \text{ms} \qquad (14)$$

We have still, however, to fit $\mathring{P}_N/P_N$ to the observed value[1] of $\sim 8 \times 10^{-10}$ s^{-1}. When condition (13) applies, our predicted value is (from equation (12))

$$\mathring{P}_N/P_N \simeq -\,0.18 \times 10^{-12}\ \mu_{30}^{-4/3}\ \Omega_c^{-1}\ \xi^{-2}\ T_{s7}^{\ 4}\text{s s}^1 \qquad (15)$$

independent of the mass, although still dependent on the neutron star model through ξ^{-2}. We see that $\Omega_c^{-1}\ \xi^{-2}\ T_{s7}^{\ 4} \simeq 5 \times 10^3\ \mu_{30}^{4/3}$ in order to fit the observed value. Moreover, with this result and equations (5) and (13) we deduce

$$\mathring{P} \gtrsim 4.7 \times 10^{-13}\ \mu_{30}^{-1/3}\ \text{s s}^{-1} \qquad (16)$$

and hence for the age we find

$$P/\mathring{P} \gtrsim 1.1 \times 10^{10}\ \text{s} \qquad (17)$$

Because of the arbitrary factor introduced previously into the mass limit (~ 1.5), ultimate limits are given by multiplying the limits (14), (16) by factors of 1.5 and 5 respectively, and dividing the limit (17) by a factor ~ 3.4. By taking the upper limit to the mass of stable neutron stars to be $\sim 1.7\ M_\odot$, we obtain the other limit in each case as: $P \lesssim 8.2\ \mu_{30}^{1/3}$ ms, $\mathring{P} \gtrsim 3 \times 10^{-16}\ \mu_{30}^{7/3}$s s^{-1} and $P/\mathring{P} \lesssim 2.7 \times 10^{12}\ \mu_{30}^{-2}$ s. We emphasize, however, that these limits are not very restrictive.

To obtain illustrative values we must consider how the condition $\Omega_c^{-1}\ \xi^{-2}\ T_{s7}^{\ 4} \simeq 5 \times 10^3\ \mu_{30}^{4/3}$ is likely to be met. With $T_{s7} \sim 1.5$ we require $\Omega_s^{-1}\ \xi^{-2} \simeq 10^3\ \mu_{30}^{4/3}$. Moreover, the largest value that it is feasible for Ω_c^{-1} to have is $\lesssim 10$, for then (equation (6) and $\alpha \sim 10^{-2}$) $T_{b7} \lesssim 10^{-0.75}\ T_{s7}$ and $(2\pi - \Omega_c)/\Omega_c \lesssim 60$, so that the background spectrum does not dominate the spot spectrum in the soft X-ray band. Hence we require $\xi^{-2} \simeq 10^3\ \mu_{30}^{4/3}\ \Omega_c$ with neither μ_{30} nor Ω_c very different from one. Unfortunately this value of ξ^2 suggests neutron star models (unpublished results of G. Baym and D. Pines) in the range 0.1–0.15 $M_\odot$, which is just where the surface radius (and ξ) begin to vary rapidly. However, typical values are obtained by choosing $M \simeq 0.1\ M_\odot$ (and therefore $\mu_{30} \lesssim 10^{-0.65}$ from relation (13) for which $\xi^{-2} \simeq 1.25 \times 10^2$ ($R_6 \simeq 5.9$). Therefore we only require (with $\mu_{30} \simeq 10^{-0.65}$) $\Omega_c \sim 10^{-0.23} \simeq 0.59$.

Thus, with equations (14), (16) and (17), we conclude that many of the features of Cen XR–3 can be explained in terms of a neutron star having the following typical properties: $\xi^2 \sim 10^{-2}$, $P \sim 8.5$ ms, $\mathring{P} \sim 7.8 \times 10^{-13}$ s s^{-1}, $P/\mathring{P} \sim 1.1 \times 10^{10}$ s ~ 370 yr. Moreover, with the particular choice of parameters and model that we have made ($\alpha \sim 10^{-2}$, $R_6 \sim 5.9$) we have the distance to Cen XR–3 as ~ 350 pc. These numbers are of course to be thought of only as illustrative, but they do suggest, however, that the neutron star which may underlie the X-ray activity of Cen XR–3 is younger than the neutron star associated with the Crab Pulsar NP 0532.

As a final remark we observe that with this theory we can estimate a maximum interval between spin changes as $\sim \mathcal{M}/\mathring{\mathcal{M}}$ or $\sim 2\,(-\Omega\,\mathcal{M}/E^2)\,(P/\mathring{P})$, which is $\sim 6 \times 10^5\ \overline{B}_{13}^2$ s for the model used above. This is typically ~ 2 yr ($\overline{B}_{13} \sim 10$), so that there is no difficulty in understanding why these events should have been observed.

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Cell Surveillance Model for Lymphocyte Cooperation

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A model is proposed for clonal proliferation and antibody production of B lymphocytes. It suggests that changes in the B cell surface due to specific antigen binding are detected by T lymphocytes, which then stimulate the B cell to proliferate.

THERE is now extensive evidence that two types of lymphocyte participate in humoral antibody production. In the mouse these cells have been convincingly distinguished by topographical distribution in lymphoid tissues[1], surface markers[2] and functions (review in ref. 3).

Antibody secretion is limited to cells of the B lymphocyte lineage, which are bone-marrow-derived (Bursa-equivalent) thymus-independent cells. B lymphocytes constitute the progenitor cells for clones of antibody secreting cells. A second population of lymphocytes are thymus-dependent cells (T cells) which are primarily mediators of cellular immunity but which are also required for the production of antibody by B cell clones. This paper deals with the nature of T cell function in cooperating with B cells for antibody secretion.

Cooperation between T and B cells has been studied with many antigens, one of the more useful systems being hapten–protein conjugates. This system can be manipulated so that recognition of the haptenic determinant is predominantly by B cells while T cells recognize chiefly carrier protein determinants[4]. Secondary stimulation of hapten specific B cells is found to be carrier protein specific due to a requirement for carrier primed T cells[5]. From results obtained in this system, it has been proposed that the role of carrier specific T cells is a passive antigen-concentrating device[4]. T cells are envisioned as a means of forming an antigen matrix which is a suitable stimulus for B cell clonal proliferation[6]. There is evidence that this antigen specific, but passive, T cell function is not in itself sufficient[7].

We have been able to replace carrier-specific T cells by unprimed allogeneic lymphocytes, together with antigen. This allogeneic stimulus is capable of eliciting expression of a single antibody forming clone of B lymphocytes. We interpret our results in terms of a cell-surveillance model for T cell cooperation in B cell function.

The clone (W_1) used in these studies produced a homogeneous IgG_1 kappa anti-DNP. Clone W_1 was isolated by spleen cell transfer in irradiated syngeneic CBA mice after initial priming with DNP–BGG. The clone was maintained by serial spleen cell transfer[8] and had been maintained through four generations at the beginning of our experiments. The functional marker for clone W_1 was the isoelectric spectrum of anti-DNP in serum (Fig. 1). Propagation of clone W_1 depends on the transfer of memory cells (of B cell lineage) from generation to generation. Proliferation and differentia-

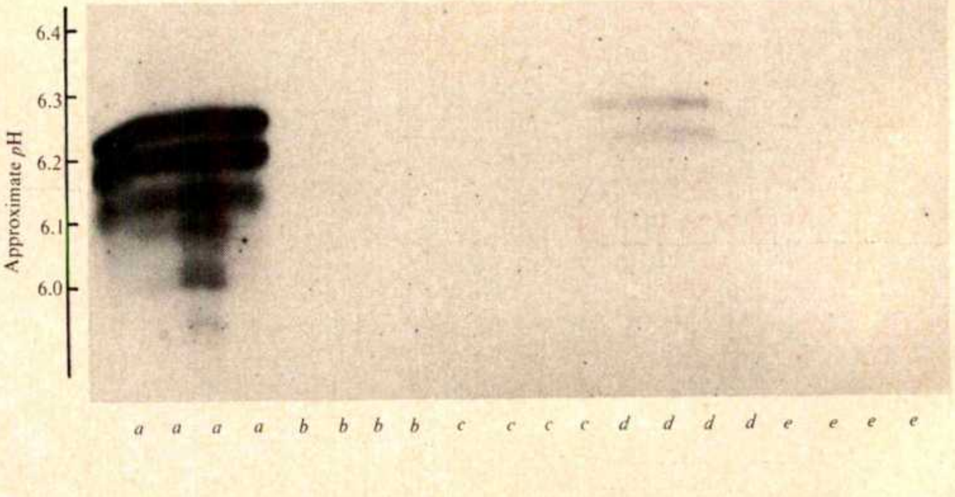

Fig. 1 Isoelectric spectrum of W_1 anti-DNP molecule in serum of irradiated CBA hosts 10 days after transfer of 6×10^6 spleen cells from a W_1 clone bearing CBA mouse together with the following: group *a*, 1 µg DNP_{12}-BGG; group *b*, 10^6 normal AKR spleen cells—no antigen; group *c*, 10^6 normal CBA spleen cells—no antigen; group *d*, 10^6 normal AKR spleen cells plus 10 µg DNP_4-OA; group *e*, 10^6 normal CBA spleen cells plus 10 µg DNP_4-OA. Each letter represents the serum of an individual recipient of the appropriate group. Isoelectric focusing was carried out in 5% polyacrylamide gel with ampholine *p*H 5–8; the specific pattern of anti-DNP molecules was detected by uptake of radioactive hapten (^{131}I-α-N-(3,5-diiodo-4-hydroxyphenacetyl)-ε-N-(2,4-dinitrophenyl)-L-lysine and autoradiography. Details can be found elsewhere[23].

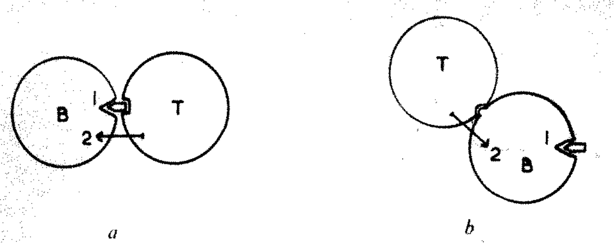

Fig. 2 Models for cell–cell interaction in the cooperation of T lymphocytes in triggering B lymphocytes to produce antibody. Cell–cell interaction effected by an antigen bridge. T and B cells have receptors specific for different determinants on the same antigen molecule. *a*, The antigen concentration-presentation hypothesis postulates multiple antigen molecules bound by T cells and presented to B cells supplying a stimulus (1) sufficient in itself for B cell proliferation and differentiation. Our cell surveillance model postulates binding of antigen by B cell receptors and subsequent recognition by T cells of exposed determinants of the bound antigen; thereupon the T cell supplies an additional stimulus (2) which is probably a soluble mitogen. *b*, Cell–cell interaction effected by histocompatibility antigens. This illustrates the system used in the present experiments to show that allogeneic T lymphocytes can replace antigen specific T cells for cooperation. The B cell requires two distinct stimuli in order to function. Antigen supplies stimulus 1 by binding to specific receptors. Stimulus 2 comes in this case from allogeneic T cells specific for B cell histocompatibility antigens with which they interact.

tion of W_1 memory cells to antibody producing cells are strictly antigen dependent, as described previously for clone E9[8].

Allogeneic Cells

Clone W_1 shows a pronounced carrier specificity. With the homologous hapten–protein conjugate (DNP_{12}–BGG) only 1 μg is needed to elicit maximal W_1 antibody production (1–2 mg antibody/ml. serum). By contrast, with 10 μg DNP_4–OA there is no production of W_1 antibody observed. Ovalbumin was deliberately chosen as a heterologous carrier in the following experiments because it is an exceptionally poor heterologous carrier in a cell cooperation system[9].

Carrier specificity in the response of W_1 memory cells to DNP–protein conjugates is due to a requirement for carrier specific T lymphocytes (as shown for clone E9[10]). Cooperation between the B and T cells has been envisaged as being mediated by an antigen bridge[4] (Fig. 2*a*). We proposed that if T cells could be brought into contact with B memory cells by a route independent of antigen (Fig. 2*b*) then production of anti-DNP by W_1 memory cells should be carrier independent. A suitable T cell–B cell interaction should be effected by mixing allogeneic lymphocytes. We chose to use spleen cells from unprimed AKR mice admixed with CBA spleen cells containing W_1 memory cells.

When 6×10^6 spleen cells from a W_1 donor CBA mouse and 10^6 normal AKR spleen cells were injected together with 10 μg DNP–OA into each irradiated CBA recipient there was a sera at 10 days after transfer as shown in Fig. 1. The combinations of cells used in this and subsequent experiments are summarized in Table 1.

This experiment shows that carrier specificity can be overcome by an allogeneic stimulus, suggesting that unprimed allogeneic T cells are substituting for the role played by carrier specific T cells. The allogeneic stimulus does not override the need for a specific DNP stimulus as there is no antibody in the absence of DNP–OA. AKR cells could not be replaced by an equal number (1×10^6) normal CBA spleen cells, or in subsequent experiments by up to 6×10^6 CBA spleen cells. The administration of antigen (DNP–OA) has in other experiments been delayed for up to 5 days after the mixed AKR–CBA/W_1 cell transfer without significantly altering the extent of W_1 antibody production. Maximal production of W_1 antibody has not yet been achieved using an allogeneic stimulus. Some killing of W_1 memory cells may occur as a result of AKR T cell aggression. However, when the group of mice receiving CBA/W_1 and AKR cells without antigen was subsequently challenged with the original antigen (DNP–BGG), production of W_1 antibody was only slightly less than in the control mice which originally received CBA cells in place of AKR cells. Thus neither W_1 memory cells nor carrier primed T cells have been extensively depleted.

Allogeneic Stimulation of B Memory Cells

We then tested whether allogeneic lymphocytes could stimulate B memory cells in the absence of syngeneic carrier-primed T cells. We therefore eliminated syngeneic T cells from CBA/W_1 spleen cells before transfer with and without AKR spleen cells. CBA T cells were killed by treatment with AKR-anti-θ_{C3H} antiserum together with complement[2]. The surviving population of CBA/W_1 B cells after transfer did not produce any W_1 anti-DNP in response to DNP–BGG (10 μg). This result exactly confirms that obtained with clone E9; in that case it was shown that the anti-DNP response could be restored by the addition of carrier primed syngeneic spleen cells. The addition of 10^6 unprimed AKR spleen cells to 4×10^6 CBA/W_1 spleen cells pretreated with anti-θ_{C3H} and complement partially restores the production of W_1 anti-DNP in response to DNP–BGG (10 μg). The level of production was very similar to that in the heterologous carrier experiment (Fig. 1). When the carrier specific T cell stimulus is replaced by an allogeneic stimulus, W_1 memory cells respond equally well to DNP on either the original carrier, BGG or on OA. There is, however, an absolute need for specific antigenic stimulus in addition to the allogeneic stimulus.

Nature of the Allogeneic Stimulus

Though CBA and AKR mice are identical at the major histocompatibility locus ($H-2^k$), they probably differ in several minor transplantation antigens. This is clearly shown by grafting skin between members of the two strains. The mean survival time of AKR skin on CBA recipients and vice versa was 14 days and 14.5 days, respectively. Graft versus host reaction was demonstrated by increased mortality after injecting normal AKR spleen cells into sublethally irradiated CBA mice. Death occurred much earlier if AKR spleen cells from animals previously sensitized against CBA transplantation antigens were used. The graft versus host reaction by 10^6 normal AKR cells is mild. This may be a major factor in

Table 1 Cells Used in the Experiments of this Study

Immunogen	CBA/W_1 cells * No./recipient	Additional cells CBA † AKR † No./recipient	No. of responding recipients per group ‡
1 μg DNP_{12} BGG	6×10^6		4/4
10 μg DNP_4 OA	6×10^6		0/4
10 μg DNP_4 OA	6×10^6	10^6	0/4
10 μg DNP_4 OA	6×10^6	10^6	3/4
None	6×10^6	10^6	0/4 [3/4¶]
10 μg DNP_{12} BGG	4×10^6 W_1—B§		0/4
10 μg DNP_{12} BGG	4×10^6 W_1—B§	10^6	3/4

* Spleen cells from a W_1 clone bearing mouse.

† Spleen cells from unprimed CBA or normal AKR mice.

‡ Cell mixtures with or without antigen (total volume: 0.2 ml.) injected into the tail vein of previously irradiated (660 r) CBA mice. Recipients bled 10–12 days after transfer. Antibody assayed by the isoelectrofusing method[23].

§ W_1 spleen cells treated with AKR anti-θ_{C3H} antiserum and complement.

¶ Challenged with 10 μg DNP_{12} BGG 17 days after transfer.

Abbreviations: dinitrophenyl-bovine gammaglobulin (DNP_{12} BGG), dinitrophenyl-ovalbumin (DNP_4 OA). Subscripts refer to mol of hapten/mol of protein.

permitting us to see the allogeneic stimulus of W_1 memory cells without overwhelming cytotoxic effects.

Effector T lymphocytes in graft versus host are capable of producing a range of soluble factors (lymphokines); one product is a mitogenic factor[10]. This mitogenic factor is the most reasonable candidate for the T cell stimulus required in addition to antigen for the proliferation and differentiation of B memory cells.

Evidence that helper cells act through a soluble factor comes from studies on *in vitro* antibody synthesizing systems. In the restricted micro-environment of a culture vessel, T cells primed against one species of foreign erythrocyte can "help" an antibody response directed against non-cross-reacting erythrocytes[11]. Both types of erythrocyte must be present but no antigen bridge can bring T and B cells together. As this type of effect cannot be engineered *in vivo*, the soluble stimulus has apparently a short range of action.

In guinea-pigs primed with DNP–OA, injection of allogeneic lymphoid cells stimulates synthesis of antibodies to both hapten and carrier in the absence of a secondary administration of antigen[12]. The anti-DNP response in these animals could be greatly enhanced by a DNP-heterologous-carrier-protein conjugate. These workers showed that the allogeneic effect was a result of graft versus host reactions but could not show an absolute requirement for antigen[12].

Cell Surveillance Hypothesis

On the basis of our studies and others quoted above, we propose a model to explain T cell cooperation in terms of the other known functions of T lymphocytes. Thymus dependent lymphocytes are mediators of cellular immunity. These cells are involved in such reactions as delayed-type hypersensitivity and graft rejection. Burnet has advanced the idea of surveillance as the basic role of T cells[13]. They operate by scanning the antigenic pattern of the body's cells. Cells with altered antigenic structures (such as certain cancer cells) are recognized as foreign and subsequently killed. One of the particular features of this system is that recognition and elimination are brought about by direct or very close cell–cell contact and that circulating humoral antibody is not involved.

The role of T cells as helpers in the B cell antibody response also involves cell–cell interaction[4], which is usually mediated by antigen (Fig. 2*a*).

Recent evidence[14] supports the idea[15] that carrier specific T helper cells are identical to delayed-type hypersensitivity effector cells. Our studies clearly show that cooperation can be achieved when T cells contact B cells through histocompatibility specificities (Fig. 2*b*). We conclude that for clonal proliferation and antibody production B memory cells require two distinct events: (1) a specific antigenic stimulus, (2) a T lymphocyte mediated stimulus, probably of a mitogenic nature.

We envisage the normal sequence of events in a secondary response to a thymus-dependent antigen as follows. Antigens are firmly bound to specific receptors of B cells which are more adequately equipped for this purpose than T cells in the sense that there is probably a higher density of receptors on their membranes[16,17]. Bound antigens will alter the antigenic composition of the B cell membrane. We assume that under normal conditions T cells are constantly scanning all other cells including B cells. Surveying cells with appropriate receptors will recognize as foreign an immunogen bound to specific surface receptors on B lymphocytes. The T cells then release a factor providing a stimulus to the B cell for clonal proliferation.

In the hapten-carrier system, with low hapten substitution, all haptenic groups can be bound by B cell receptors leaving only carrier determinants to be surveyed by T cells. This explains the requirement for carrier specific helper cells. The surveillance hypothesis can also offer an explanation why hapten-carrier cooperation is unaffected by 100–200-fold excess of soluble carrier proteins[9]. The antigen concentration hypothesis would predict that the formation of a hapten–protein matrix on protein specific T cells would be very susceptible to inhibition by carrier protein. On the contrary, the surveillance model may require as few as one antigenic bridge between B cell and T cell.

Our hypothesis makes it unnecessary to devise two divergent mechanisms for T cell action: one for killing foreign target cells and a different one for T cell : B cell cooperation. In our system of a single CBA B cell clone with normal AKR spleen cells, a delicate balance between killing and stimulation of B cells has apparently been established. When the number of normal AKR spleen cells was increased or spleen cells were used from animals previously sensitized against CBA transplantation antigens or even primed with ovalbumin and *Bacillus pertussis*, most of the animals died within the first week after transfer. Those recipients surviving for a longer period had no detectable serum antibody. It is reasonable to assume that in this model, killing and stimulation are two manifestations of the same fundamental process which consists of AKR T cells surveying CBA target cells including W_1 B cells.

The cell surveillance model is consistent not only with the data on positive T cell cooperation but also with recent evidence suggesting negative cooperation[18,19] and other controlling functions mediated by T cells[20]. Our results can readily explain the reported abrogation of sheep erythrocyte tolerance in rats by administration of allogeneic lymphocytes[21]. Another model system which can be interpreted in terms of our data is chronic allogeneic disease in F_1 hybrids where parental lymphocytes induce host B cells to proliferate and produce auto-antibodies[22].

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LETTERS TO NATURE

PHYSICAL SCIENCES

Observation of Volcanic Eruption by an Infrared Radiation Meter

On September 18, 1970, eruptive activity was initiated from one of the central cones of Akita-komaga-take. The eruption continued for almost 4 months, though mild in activity, and a lava flow extended towards the south-west of the cone.

Akita-komaga-take is located at the northern part of northern Honshu, Japan, and is 1,637 m in altitude. The volcano has a horseshoe-shaped crater at the summit within which three central cones exist. One of the three cones, Medake (1,500 m in altitude), has six explosion pits on its summit. The known records of eruption are 1891, 1902 and 1932, all of which were known as steam eruptions.

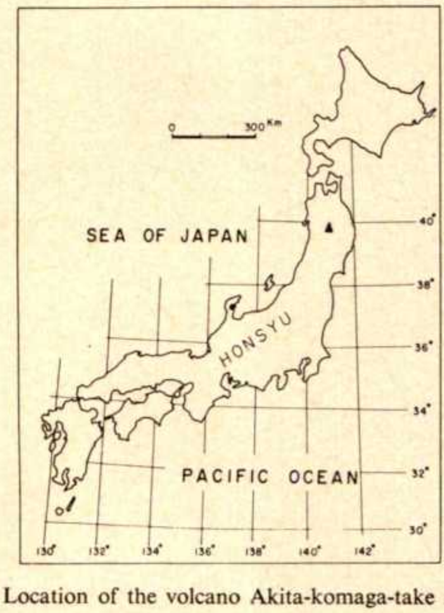

Fig. 1 Location of the volcano Akita-komaga-take indicated.

The recent eruption began from one of the vents of the summit of Medake. The eruptive manifestation is intermediate between Strombolian and Vulcanian type. During the early stage of the activity, the eruption took place at intervals of several minutes. An eyewitness observation has been made occasionally at one of the peaks of the Somma O-dake, 500 m north of the eruptive vent, from which the lava head of the vent was clearly observed without any risk from falling ejecta.

We observed the eruption with an infrared radiation meter in order to determine the accurate time of the eruption and to find a correlation between the pattern of infrared radiation and the earthquakes associated with the particular eruption.

One week after the beginning of the eruption, we set up eight seismometers on the western flank of the volcano, along the line of the steepest slope. Two of them were monitoring seismographs, with smoked paper recording, and the others were temporary, monitoring by a data recorder of magnetic tape or an optical oscillograph with high magnification.

Detailed results of the seismic observation are not described here. But particularly interesting results from the seismic observation are that most of the volcanic earthquakes were those associated with respective eruption. Volcanic earthquakes of different origin have been quite few in number.

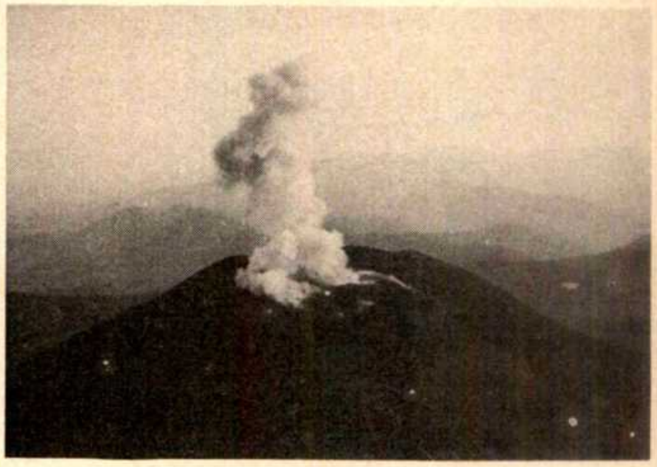

Fig. 2 Minor eruption of Akita-komaga-take.

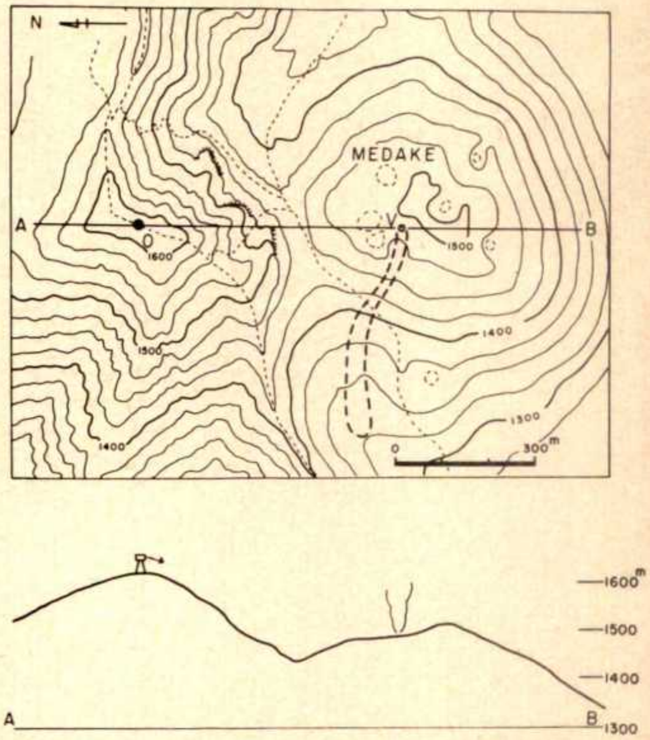

Fig. 3 Topography of Akita-komaga-take and its profile along the line A–B. Location of an infrared radiation meter and the eruptive vent is indicated by O and V, respectively. Dotted line is a rough sketch of the lava flow in its early stages.

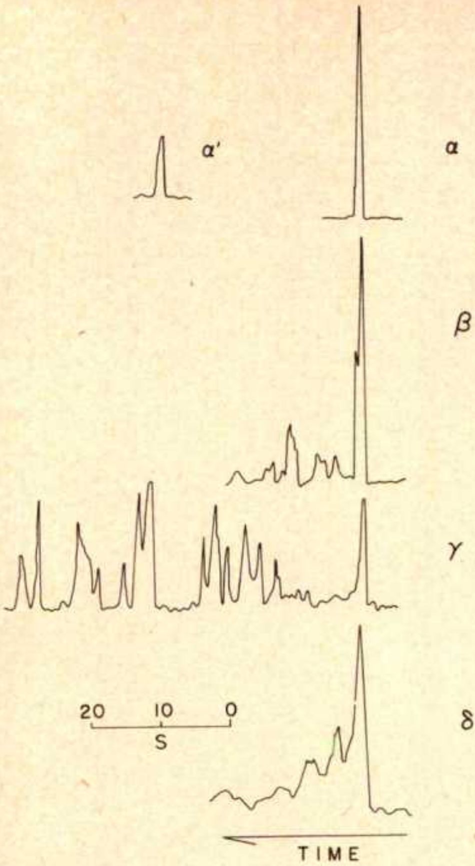

Fig. 4 Types of eruption based on the IRM records.

Besides seismic observation, we set up a portable infrared radiation meter (IRM) on one of the peaks of the Somma O-dake, 500 m from the eruptive vent.

The optical window of the IRM is between 1.8 μm and 2.5 μm. The output signal was recorded by a pen-writing milli-voltmeter. The IRM is designed for industrial use, so the field of view is not narrow enough to observe the surface temperature of the lava head of the vent, or that of the eruptive cloud, at such distances. The observed area was estimated as roughly 6 m in diameter at a distance of 500 m. Therefore the recorded temperature might be the average temperature of the field of view. Time marks of seconds and minutes from the crystal clock were fed onto the recording paper, for which a paper speed of 3 mm/s was selected. A Honda 300 W gasoline generator was used as the power supply.

We obtained many records of eruptions, from which we can classify the eruptive manifestation as follows.

Type α: single eruption ejecting lava fragments and ash with volcanic cloud and strong sound; α': small single eruption, mostly of gas emission; β: single eruption followed by successive minor eruptions ($\beta = \alpha + \alpha'$); γ: successive minor eruptions ($\gamma = n\alpha'$); δ: ejection of lava fragments with only a small initial velocity. No earthquakes are associated.

Typical records corresponding to the above classification are shown in Fig. 4. The amplitude of the record is proportional to the surface temperature and we can obtain the temperature scale if we assume the emissivity of the source. Because of the relatively wide field of the optical system, we could not determine the actual surface temperature of the lava head of the vent or of the volcanic cloud. In this connexion, the ordinate should be read as the modified temperature scale. It should be said, however, that the integration of the record provides a quantity proportional to the thermal energy released by the particular eruption.

In the early stage of the activity, the IRM record showed a large amplitude and long duration compared with that of the later stage. An example for both stages is shown in **Fig. 5**, in which the change in character of eruptive activity with time is well shown. It may be said that observation by IRM provides a precautionary measure of the future volcanic activity.

To investigate the nature of earthquakes associated with volcanic eruption, simultaneous observation of earthquakes and infrared radiation has been carried out. Earthquakes were recorded by a four-channel data recorder with three vertical seismometers located along the steepest slope of the volcano, while the IRM was operated on the summit. Seismographs should have been operated on the summit in order to utilize the crystal clock which was fed to the IRM. But, owing to the difficulties of operating seismographs on the summit, we were forced to make a simultaneous observation with two crystal clocks at different places. In this circumstance, examination of the difference in the time of the first onset of both records involves error, even if we check the two clocks. Certainly, these problems are very important in the

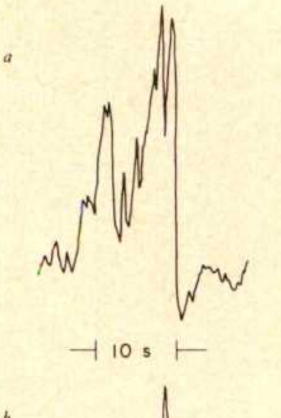

Fig. 5 Eruption recorded by the IRM in the early stage (*A*) and later stage (*B*).

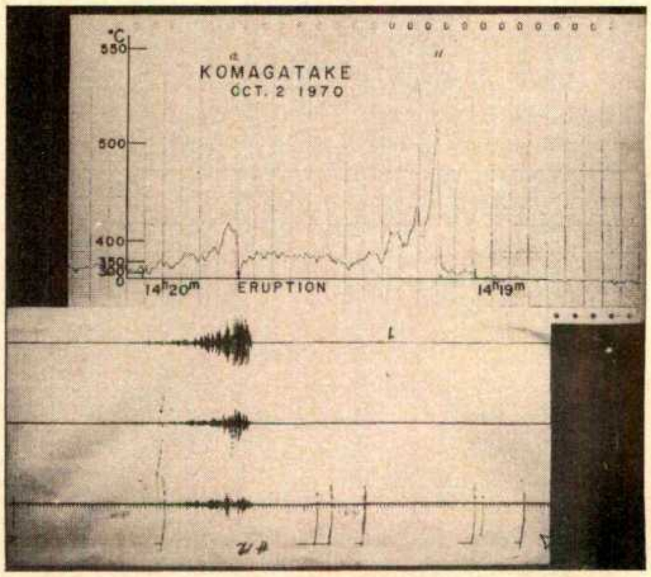

Fig. 6 Upper record of IRM shows two eruptions. An associated explosion earthquake was recorded only for the later eruption.

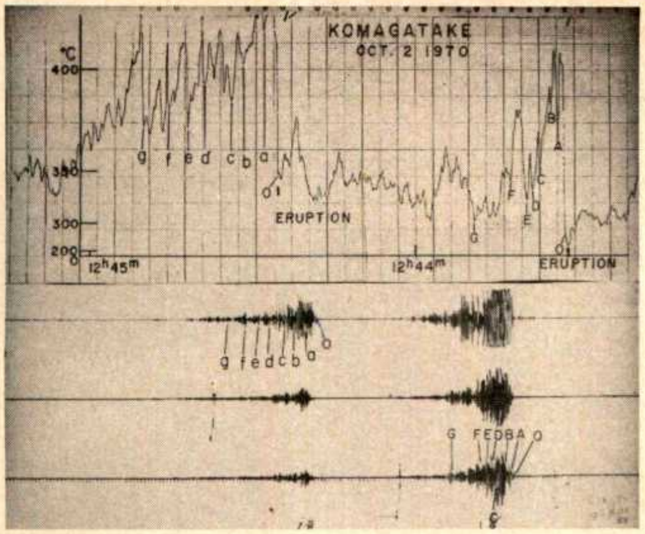

Fig. 7 Correspondence of phases between IRM record and seismogram.

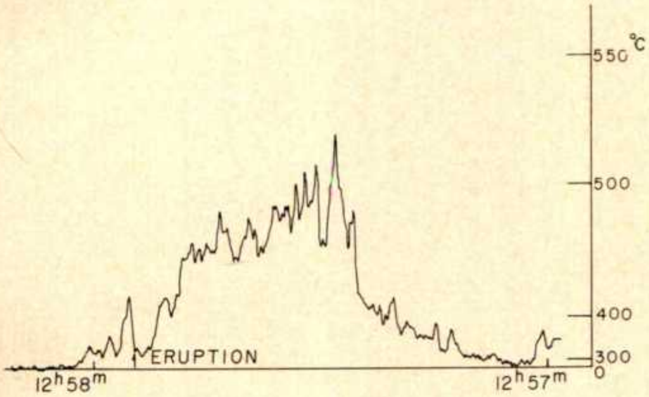

Fig. 8 IRM record of the swelling of the lava head of the vent before the eruption (October 2, 1970).

study of the eruptive mechanism, that is, the depth at which the explosion earthquakes occur. In the case of the present observations, we obtained insufficient results. But, relatively speaking, the time difference is not always the same. It implies a difference in the focal depth of explosion earthquakes for the different eruptions.

The following results are most interesting in regard to the investigation of eruptive mechanisms.

(1) In Fig. 6, two eruptions are recorded by IRM (upper part), eruption No. 11 and No. 12. The explosion earthquakes were only recorded for No. 12 eruption. The time corresponding to the onset of eruption No. 11 is indicated by an arrow on the seismogram. It is clear, from eyewitness observation, that No. 12 was an eruption of the type which ejected lava fragments only. It was found that this type of eruption was not associated with earthquakes.

(2) In Fig. 7, two eruptions are recorded on both an IRM and a seismogram. As can be seen from the IRM record, each eruption is made up of several successive minor eruptions. Major phases are marked by alphabetical letters.

On the other hand, if we make the time of onset of the IRM equal to the time of the first arrival of the seismogram, and transform the time of phases (*A*, *B*, *C*, . . . , *a*, *b*, *c*, . . .) of IRM to the seismogram, we can find the distinct phases, as can be seen in the lower part of Fig. 7. From this fact, later phases of explosion earthquakes, so far as we observed, are found to be associated with the respective succeeding eruptions.

Furthermore, in Fig. 7 the thermal energy released by the second eruption is larger than that of the first eruption. On the other hand, earthquakes associated with these eruptions show the opposite relation—energy released as seismic waves is larger for the first eruption than the second eruption. This implies a considerable difference in the partition of eruptive energy for the two eruptions.

(3) IRM records show another interesting feature. Before a particular eruption, the head of the lava column at the vent shows a vertical oscillation which was clearly observed by the IRM, as shown in Fig. 8. This example shows the upward movement of the lava column in the vent, some 40–50 s before the eruption. The IRM record indicates gradual swelling of the lava column, involving vertical oscillation. This pre-eruptive stage is associated with neither earthquakes nor harmonic tremor.

I thank Asahi Electron Optics Laboratory, Tokyo, for the IRM.

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Radiography of Diffusion in Gels

IN our study of crystal growth in gels, we have developed a simple technique for monitoring the concentration changes of appropriate ions and molecules in translucent and opaque media by radiography.

The observation of diffusion in aqueous gels by optical methods, for example, the Goüy method[1], is hampered by the absorption, inhomogeneity and frequent opacity of the medium. Indicator methods[2] require the presence of an indicating reagent which may participate in the diffusion process and which does not necessarily give strict concentration dependence. Radioactive tracer methods have been used for this purpose in the past[3] but they entail the use of special reagents and destruction of the medium in order to count specific activity in zones throughout the gel. Other methods involve measurement of the average concentration of diffusant throughout the gel

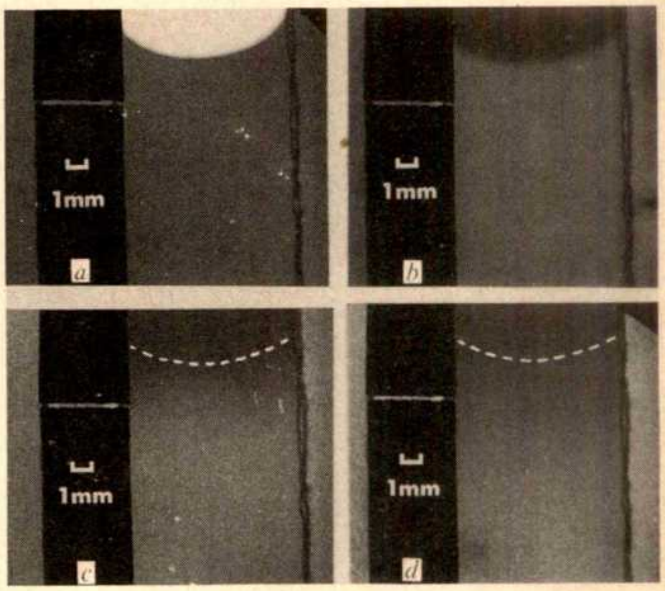

Fig. 1 Radiographs of 1% agar gel. *a*, With air above the boundary; *b*, at $t=0$ min with 0.5 M calcium chloride solution above the boundary; *c*, at $t=38$ min; and *d*, at $t=140$ min. Width of meniscus = 8 mm. The exposures of the prints reproduced here have been adjusted to accentuate the contrast in the gel itself in each case.

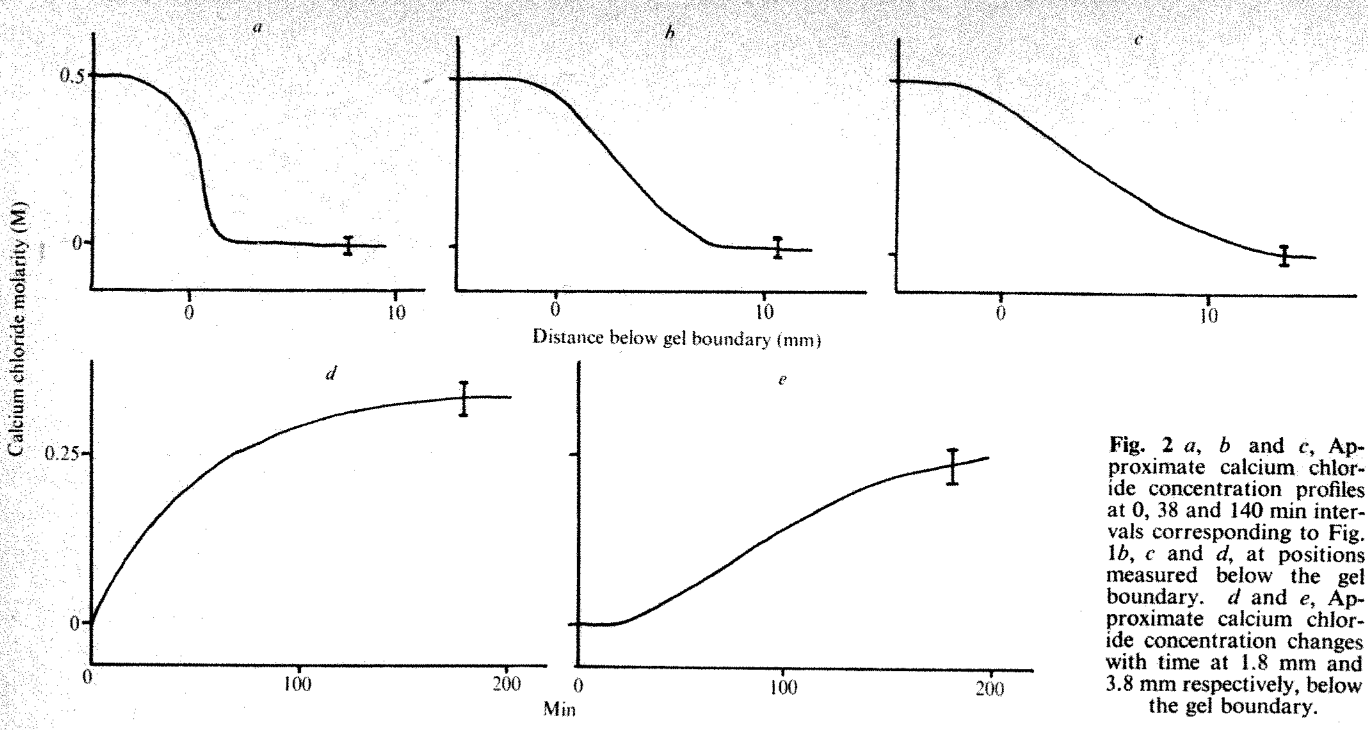

Fig. 2 *a*, *b* and *c*, Approximate calcium chloride concentration profiles at 0, 38 and 140 min intervals corresponding to Fig. 1*b*, *c* and *d*, at positions measured below the gel boundary. *d* and *e*, Approximate calcium chloride concentration changes with time at 1.8 mm and 3.8 mm respectively, below the gel boundary.

or in the diffusing solution[3,4]; our method provides concentration values at any instant anywhere in a projection of the system.

The diffusion system was contained in a small parallel sided cell 6 × 2.5 cm and 0.32 cm thick, made of 1/16 inch (0.158 cm) 'Perspex' and divided into several compartments. Such a cell is susceptible to variation in thickness due to buckling and bending in preparation, however, and as such is not recommended for quantitative use. A glass cell of similar dimensions can be made to a high degree of accuracy but requires longer exposures owing to the poor X-ray transmission characteristics of most glasses. A conventional crystallographic X-ray tube with a copper target run at 18 kV and 2 mA was used to provide a circle of quasi-monochromated X-rays 6.25 cm^2 in area, 40 cm from the tube. For the particular cell described exposures of the order of 10 s were required for Kodak fast dental film.

Fig. 1*a* shows the positive of a radiograph of a double cell containing a 1% agar gel. The grey shadow below the meniscus represents the gel with air above it. The dark shadows on the left of the gel are from lead strips which form an intensity and, spatial reference. On the extreme left the shadow of the second compartment containing distilled water is visible and, on the right, the shadow of a 'Perspex' spacer at the edge of the cell. The intensities of the latter two shadows, together with that of a 0.0233 mm nickel strip elsewhere on the film, taken relative to the lead shadow, provide a means of standardizing and scaling different films of varying exposure. By using a combination of absorbers of different thickness it is possible to extend this method to obtain scale factors to any desired degree of sophistication.

In Fig. 1*b* a 0.5 M calcium chloride solution has been added above the gel; it appears dark because of the absorption of calcium chloride ions. Figs. 1*c* and *d* show succeeding radiographs at 38 and 140 min intervals from Fig. 1*b* respectively, in which the diffusion of calcium chloride into the gel at 20° C is clearly seen. From a microdensitometer trace of such radiographs it is possible to measure the intensity variation, relative to the internal absorption standards, along the path of the diffusant anywhere on the projection of the gel sample. By obtaining the relative intensities of standard solutions of the diffusant in the cell used from radiographs, the microdensitometer of the diffusion process can be converted to a concentration profile throughout the gel, with a reproducibility of about 7% down to a concentration of 0.005 M for calcium chloride. Use of a monochromated X-ray source would allow direct calculation of the diffusant concentration from radiograph intensities, using standard atomic absorption coefficients[5].

Figs. 2*a*, *b* and *c* show concentration profiles corresponding to Figs. 1*b*, *c* and *d*, taken perpendicular to the gel meniscus, at its centre. From a series of concentration profiles, the concentration changes at a particular position in the gel and the movement of a particular concentration contour with respect to time can be obtained. The concentration changes at two positions in the agar gel are shown in Figs. 2*d* and *e*. By using the well known Fourier series solution to Fick's second law of diffusion[1] it is possible to extract a diffusion coefficient from the observed concentration values for the diffusant in the gel medium. No diffusion coefficients are quoted, as preliminary results obtained using a 'Perspex' cell were inconsistent and, as described, we feel more dependable information can be obtained using glass cells.

The method outlined is simple and has been used to obtain preliminary comparative information on the diffusion of ions in a wide variety of gels. We intend to use this method to monitor the growth and dissolution of crystals in gels, especially in connexion with mineralization and demineralization in biological systems, and also in the presence of electric and magnetic fields and as a function of temperature. We hope that it may also be possible to make similar studies of the behaviour of organic crystals in appropriate systems by methods of this kind and suggest that the method may be applicable to a wide variety of diffusion systems, particularly in solution and hot gas flow streams.

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Internal Friction in Moon and Earth Rocks

RECENT measurements of the quality factor, Q, for mechanical vibrations generated by dropping parts of the Apollo lunar module and by moonquakes[1] indicate that the Q of the Moon for these vibrations is of the order of 3,000, but seismological measurements of the Earth's rocks indicate Qs of 110 for the outer mantle[2], with higher values for the inner mantle. It is the purpose of this report to indicate that these lunar results are consistent with a dislocation source for internal friction.

A dislocation mechanism has been discussed[3] which gives an internal friction independent of the frequency for low frequencies and a Granato–Lücke type performance at higher frequencies. The complete normalized internal friction curve is shown in Fig. 1. The normalized frequency ratio (ω/ω_0) is determined by the angular measuring frequency ω divided by $\omega_0 = \mu b^2/Bl_A{}^2$ where μ is the shear stiffness, b the Burger's distance, B the drag coefficient which measures the force proportional to the velocity exerted on dislocations by phonons and electrons, and l_A is the average distance between impurity pinning points for an exponential distribution. The normalized internal friction ratio determines the ratio of Q^{-1} to $\bar{N}Rl_A{}^2$ where $\bar{N}$ is the total length of dislocation per cm^3, and R is an orientation factor which determines the ratio of the shearing stress in the glide plane to the stress in the mode of vibration. For a Young's modulus type of vibration, a reasonable value is $R=0.25$. Assuming, as will be shown likely, that Moon rocks are similar to impure metals and alloys, which have $l_A \doteqdot 3\times10^{-5}$ cm, gives a Q of 3,000 when $\bar{N}=5\times10^7$, a value consistent with alloys and impure metals.

Two measurements[4] have been made on Westerley granite and Pennsylvania slate which agree with the form of the theoretical curve of Fig. 1. A third rock Solenhofen limestone has recently been completed with the results shown in Fig. 2. The lower frequency part of this curve and the squares of the high frequency measurements were made by a continuous wave measurement with two equal transducers cemented to a half wave specimen of rock. The resonant frequency determines the elastic modulus while the width of the resonant curve determines the internal friction Q^{-1}. The crosses show measurements by a pulsing method which also gives the velocity as 5.65×10^5 cm s^{-1}. The triangles and circles show other measurements of the same limestone[5] (triangles) and a different limestone[6]. The agreement is good up to 5 MHz. Above this frequency, scattering losses become large enough to make measurements questionable. As can be seen the dislocation loop length is in the order of 1.9×10^{-4} cm while the number of dislocations is about 10^7 cm^{-2}. As will be shown here, these values are associated with the numbers expected for free surfaces where l_A is effectively larger and $\bar{N}$ smaller than for a continuous medium.

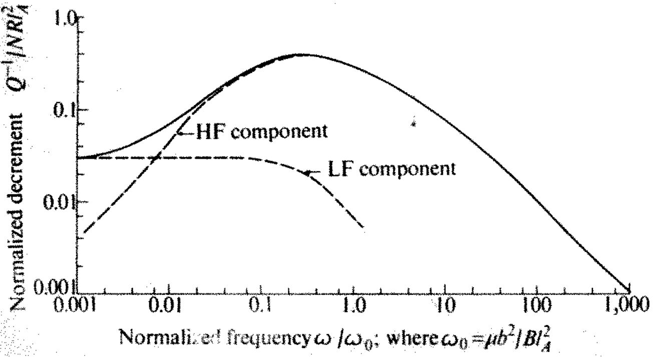

Fig. 1 Normalized internal friction curve against normalized frequency for an exponential distribution of pinning points.

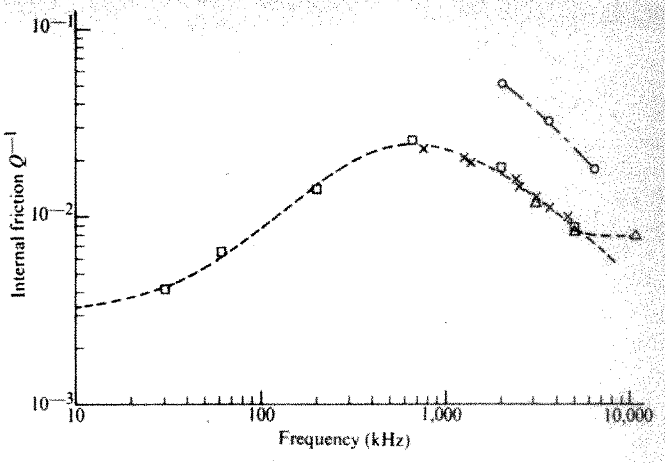

Fig. 2 Internal friction measurements for Solenhofen limestone. ○, Krishnamurthi and Balakrishna; △, Peselnick and Zeitz; □, continuous wave measurement; ×, pulsing measurement; - - -, theoretical.

For a rock most of the internal friction is connected with the grain boundaries as can be seen from the fact that hydrostatic pressure reduces the internal friction by a factor of 10 or more[7,8]. A model is used here for which a grain boundary is represented by a series of spherical surfaces having a shearing modulus $\mu(1+j/Q_1)$ pressing on each other, while the interior is represented by a solid having a stiffness $\mu[1+j/Q_2]$. Making use of the Hertz theory of contacts and Mindlin's[9] calculations of the displacement of a set of convex surfaces, then for an applied alternating force T we find, for the sidewise displacement dx_2,

$$dx_2 = \frac{(2-\sigma)T}{8a\mu(1+j/Q_1)} \tag{1}$$

The tangential force T is related to the applied shearing stress T_6 by

$$T_6 = T(\pi a^2)n_0 \tag{2}$$

where a is the Hertz radius of contact, and n_0 the total number of contacts per cm^2. The Hertz radius of contact is determined by

$$a = \sqrt[3]{\frac{3}{4}\ Nr\left(\frac{1-\sigma}{\mu}\right)} \tag{3}$$

where r is the radius of the spherical contact surfaces and N the normal force on each contact. The product Nr can be eliminated by considering the thickness t_1 of the layer $r\theta^2$ and the area $\pi r^2\theta^2$ where θ is half the angle determined by the radius of curvature r. Then

$$Nr = T_1/n_0\pi t_1 \tag{4}$$

where T_1 is the sum of the pressure holding the rock together, T_{1_e}, plus the applied hydrostatic pressure. Introducing all these values the sidewise displacement is

$$dx_2 = \frac{(2-\sigma)}{6(1-\sigma)}\ \frac{T_6 t_1}{T_1(1+j/Q_1)} \tag{5}$$

To the displacement of the intermediate layer we have to add that in the two outside layers which result in

$$dx_1 = \frac{T_6 t_2}{\mu(1+j/Q_2)} \tag{6}$$

Making use of the fact that Q_1^{-1} and Q_2^{-1} are small, the ratio between the applied shearing stress T_6 and the shearing strain

$$S_6 = \frac{2(dx_1+dx_2)}{t_1+t_2}$$

is

$$\mu_T = \mu[1+t_1/t_2]/(1+A);\ Q_T^{-1} = Q_2^{-1} - \frac{A(Q_2^{-1}-Q_1^{-1})}{1+A} \tag{7}$$

where

$$A = \frac{(2-\sigma)}{6(1-\sigma)}\,\frac{\mu}{T_1}\,\frac{t_1}{t_2}$$

The fact that lunar rocks studied on Earth[10] have a Q of only 10 to 100 is not in contradiction with the high Q measured on the Moon. As shown by equation (7) the Q measured for rocks in the laboratory is mostly determined by grain boundaries and cracks between various parts. It is not until the pressure is high enough to eliminate these that the Q is determined by the internal structure of the rock. Hence the measurements of Warren *et al.*[10] in no way contradict the ideas expressed here.

Using measurements[11] of the shear stiffness of Westerley granite (Fig. 3) it is found that $T_{1_0} = 3 \times 10^8$ dyne cm^{-2}; $t_1/t_2 = 1.7 \times 10^{-3}$ and $\mu = 3.57 \times 10^{11}$ dyne cm^{-2}. Hence for no external pressure the internal friction is

$$Q_T^{-1} = 0.545\, Q_2^{-1} + 0.455\, Q_1^{-1} \qquad (8)$$

while for high pressures it is equal to Q_2^{-1}, the value for the medium. Using the above values and Q_1^{-1} equal to 1.1×10^{-2} to agree with the torsional wave measurements of Birch and Bancroft[7] on Rockport granite (550×10^{-5} at 200 bar and 60×10^{-5} at 4 kbar) the value due to the boundary is less than 2×10^{-4} at 10 kbar while Q_2^{-1}, the internal friction of rocks without flaws, is less than 2×10^{-4}. Hence granite under pressure has internal friction values of the order of that found for Moon rocks. Because all the seismological measurements and the Moon rock measurements are for hydrostatic pressures large enough to eliminate the effect of the boundary, we are dealing with the internal friction of the medium itself. The question then is why the internal friction of the Moon rocks is so much lower.

The answer seems to be that the shearing stress associated with the ellipticity of the Moon (about 10^7 dyne cm^{-2}, ref. 12) is insufficient to generate new dislocations by the Frank-Read mechanism whereas the stress in the Earth's crust (from 6×10^7 to 10^8 dyne cm^{-2}) is large enough to generate new dislocations. A Frank-Read mechanism starts to function when the applied shearing stress—perhaps tectonic in origin—is

$$T_6 = \frac{\mu b}{l_N} \qquad (9)$$

where l_N is the network length, that is, the distance between dislocation joins. The Frank-Read source will operate until the length l_N is equal to $\mu b/T_6$. If some of these loops anneal out, the mill is started again until l_N is determined by $\mu b/T_6$. Some idea of l_N can be obtained for brass from the data of Fig. 4, which shows the internal friction as a function of the longitudinal strain. At about 3×10^{-4}, the dislocation mill starts to move as can be seen by the presence of slip bands[13]. This requires a longitudinal stress of 3×10^8 dyne cm^{-2} or, with an orientation factor of 0.25, a shearing stress of 7.5×10^7 dyne cm^{-2} which from (9) results in a network length of 1.25×10^{-4} cm. For the rock it might be somewhat larger but would not be large enough to cause the mill to operate at a stress of 10^7 dyne cm^{-2}. An even stronger argument[12] is that the ellipticity of the Moon has not changed during geological times even though it keeps the same face to the Earth.

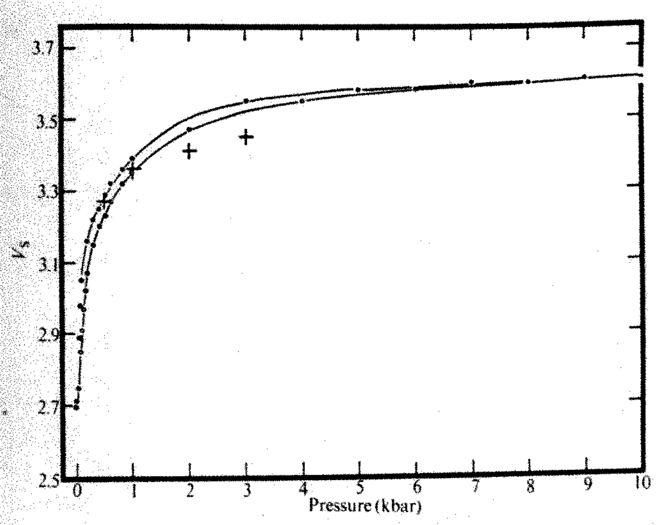

Fig. 3 Shear velocity of Westerley granite as a function of hydrostatic pressure. The lower curve was obtained with increasing pressure. Crosses represent data from Birch and Bancroft (from ref. 11).

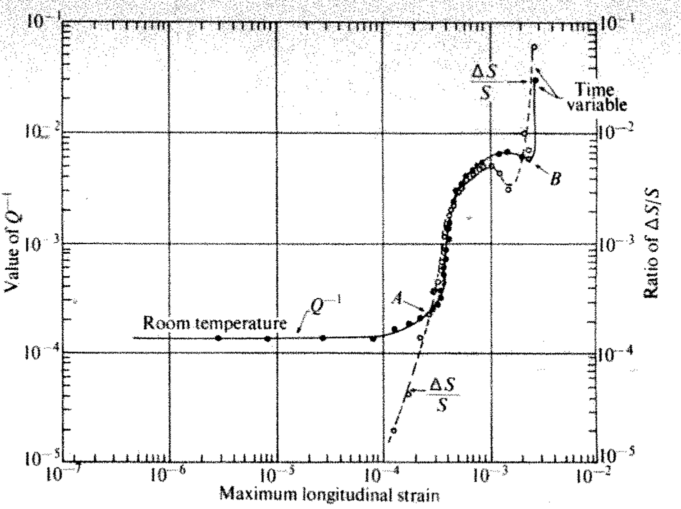

Fig. 4 Internal friction plotted as a function of the maximum longitudinal strain for brass. Slip bands begin to form at a strain of 3×10^{-4}.

For the Earth, the stresses are larger and they occur every 12 h. Thus new dislocations can be generated which will probably be pinned eventually by impurities giving the same pinning distance l_A as in the unstrained rock. The number of dislocations will continue to increase until the joins of the network reduce the network length l_N to a length such that the Frank-Read mechanism can no longer operate. A rough idea of the relation between $\bar{N}$ and l_N can be obtained from the equation

$$\bar{N} l_N^2 = 3$$

as can be seen from a figure showing the network as blocks with dislocations going straight through. For $\bar{N} = 5 \times 10^7$; l_N is 2.3×10^{-4} cm which is not long enough to start a dislocation mill on the Moon. For a Q of 110, the number of dislocations has increased by a factor 27.2 which results in a value of l_N of 4.7×10^{-5} cm. This gives a shearing stress of 1.9×10^8 dyne cm^{-2} to cut the mill off. Although all these figures are approximate, they are close to what is expected.

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Time of Formation of the Earth's Core

ACCORDING to several theories[1-3], the Earth was formed by accretion from a mixture of silicate particles and metal particles, something like those in chondritic meteorites. The accreting material may also have contained relatively small quantities of other components such as iron meteorites[4] and carbonaceous chondrites[5]. Most advocates of these theories have maintained that accretion occurred relatively slowly (over a period of about 10^8 yr), so that the gravitational potential energy was efficiently radiated away and the Earth formed in a relatively cool and unmelted condition. Subsequently, heating by long lived radioactive elements occurred, leading to melting of the metal phase and segregation of the core. Differentiation and formation of the core may thus have occurred much later than the primary accretion of the Earth. It has even been argued that core formation might not yet have proceeded to completion[1,6,7]. On the other hand, alternative theories of origin of the Earth[8-10,11] have maintained that much of the accretion of the Earth occurred in high temperature conditions and that core formation occurred either during accretion or very soon afterward. Clearly, an independent determination of the time interval ΔT_c between accretion and core formation would have a crucial bearing on these contrasting theories.

The age of the Earth, T_0, is believed to be close to 4.55×10^9 yr (refs. 12 and 13). This age is based on the discovery that the isotopic composition of modern terrestrial lead falls on the meteoritic isochron, which records a differentiation of lead relative to uranium within meteorites at this time. The mean growth curve for lead ore bodies indicates an age of 4.58×10^9 or 4.55×10^9 yr for the Earth depending on the choice of ores included in the calculation[14,15]. Both the meteorite and ore body ages assume that the lead/uranium ratio of the upper mantle–crust system had been established at T_0, and since then had remained constant to a first approximation.

In 1960, Ringwood[8] argued that formation of the core would probably alter the Pb/U ratio of the mantle because the molten iron would be expected to carry down substantial amounts of lead but not uranium. He concluded, therefore, that the 4.55×10^9 yr terrestrial event recorded by Pb/U geochronology actually referred to the date of core formation, which must have occurred very soon after formation of the Earth.

The principal assumption behind this conclusion was that during core formation the Pb/U ratio of the metal phase would be much higher than that of the silicate phase and that a substantial proportion of the total lead in the Earth would enter the core. This assumption was not accepted by Patterson and Tatsumoto[16], however, who maintained that lead would be preferentially partitioned into the silicate phase. Their calculations of mantle evolution implicitly require that either trivial amounts of lead are partitioned into the core, or that core formation occurred instantaneously 4.55×10^9 yr ago. It is not obvious that either of these implicit assumptions is necessarily true. Clearly, experimental measurements of the distribution coefficient of lead between relevant metal and silicate systems are necessary. We have carried out a series of experiments of this nature. It was difficult to perform these experiments at atmospheric pressure because lead tends to volatilize at temperatures at which the metallic iron-rich phase is molten. Accordingly, the experiments were performed at high pressures under closed system conditions, thereby preventing volatilization.

The experiments were designed as analogues of the core formation process in the Earth, as envisaged in various theories. The Earth's core is believed to contain 10–30% of one or more light elements (such as S, Si, C) in addition to iron[17-19]. According to a widely discussed current theory the Earth accreted mainly from material resembling ordinary chondrites[3,20-22] together with a small proportion of carbonaceous chondrite like material, which was the "carrier" of volatile components[5]. On this hypothesis the principal light-element component of the core would consist of sulphur with a smaller amount of carbon. We represented this model with a synthetic metal phase of composition (weight per cent) $Fe_{83}S_{15}C_2$. Another model[8,19] of core formation regards silicon as the most important light element. To test this model, a metal phase of composition $Fe_{89}Si_{11}$ was used. Finally, according to a third hypothesis[23] the Earth's core contains the primordial abundance of sulphur. In the relevant experiment, a metal phase of composition $Fe_{70}S_{30}$ was used.

The silicate phase used in the experiments consisted of simplified synthetic basaltic compositions, doped with 1,000 p.p.m. of lead (as oxide) in some runs and 100 p.p.m. Pb in others. For experiments on the $Fe_{89}Si_{11}$-basalt system, the simplified basalt composition contained no iron, whereas the other basaltic compositions used contained normal amounts of oxidized iron.

In the experiments, finely powdered samples of metal phase were mixed with silicate in the ratio 1 part (by weight) of metal to 2 parts silicate. The mixture (400 mg) was then charged into a closed alundum capsule which was placed in an internally heated piston cylinder high pressure apparatus[24]. In a given run, the sample was first subjected to the desired pressure. Temperature was then increased to 1,100° C and held for 30 min, to recrystallize and equilibrate the charge under sub-solidus conditions. The temperature was then slowly increased over a period of 1.5 h to a maximum temperature at which both metal and silicate phase were known to be molten. The temperature was held steady for 10 min, and the system was then switched off. Pressure was released after cooling and the samples removed from the apparatus. The metal was usually found to have sunk to the bottom of the capsule as one or more globules. Metal and silicate phases were crushed and separated magnetically. The concentrations of lead in coexisting metal and silicate phases were then determined by isotope dilution with Pb runs as PbI_2^+ (ref. 25). Blanks were approximately 20 ng per analysis.

Distribution coefficients for lead between metal and silicate phases (K^m's) were obtained for each experiment. The distribution coefficient is the ratio of Pb concentration in the metal to Pb concentration in the silicate phase. Results are shown in Table 1. They are sufficiently consistent to support the belief that equilibrium was approached. The fact that all lead was initially in the silicate phase means that our distribution coefficients represent minimum values.

A series of runs was made at 10 kbar. These illustrate the relation between distribution coefficients and metal phase

Table 1 Distribution Coefficients for Lead between Metal and Silicate Phases

Metal phase	Pressure (kbar)	Maximum temperature (°C)	*K* metal/silicate
$Fe_{70}S_{30}$	10	1,400	9.8, 12.4
$Fe_{89}Si_{11}$	10	1,400	3.7, 3.8
$Fe_{83}S_{15}C_2$	10	1,400	1.9, 2.0, 2.1
$Fe_{83}S_{15}C_2$	5–40 12 runs over 5 kbar intervals including repeats	1,350–1,650	1.4 to 2.9 Most probable value 2.5±0.5

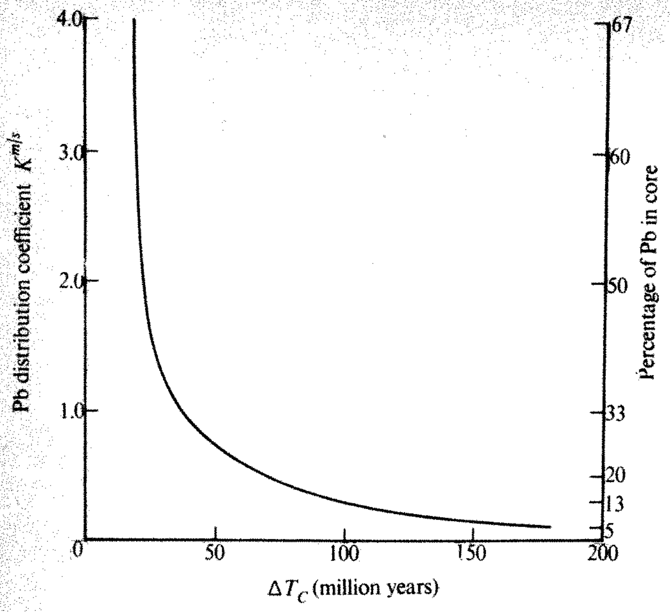

Fig. 1 Relationship of time delay for core formation after accretion of Earth, ΔTc, with the distribution coefficient for lead between metal and silicate phase, $K^{m/s}$. Time of accretion is taken as 4.55×10^9 yr. Isotopic composition of upper mantle lead is taken as that from tholeiites dredged from floor of Pacific Ocean[28].

compositions (Table 1). It is seen that the coefficients for $Fe_{70}S_{30}$ and $Fe_{89}Si_{11}$ are higher than for the $Fe_{83}S_{15}C_2$ alloy. Evidently carbon has the effect of increasing the activity of lead in the alloy. A further series of runs was made over a pressure range from 5–40 kbar. The temperature at which equilibration was reached in these runs is not known precisely because the metal (which melts at a lower temperature than the silicate) tends to segregate and sink to the bottom of the capsule when the basalt is melting. Thus the P, T conditions under which equilibration occurred probably correspond approximately to the liquidus of basalt or to the solidus of mantle peridotite[26]. Conditions of segregation of metal phase are thus analogous to those which may have occurred during core segregation in the Earth. Three runs were carried out at 15 kbar and at maximum temperatures of 1,450° C, 1,500° C, 1,600° C. The scatter was large and no systematic effect of temperature on distribution coefficient was seen. Also, no systematic effect of pressure on the distribution coefficient in the range 5–40 kbar was evident in the runs using the $Fe_{83}S_{15}C_2$ alloy. There is some scatter in the results, probably due to failure to attain complete equilibrium which would reduce the distribution coefficient values. It is probable, therefore, that the higher values obtained are more nearly correct and our estimate for the distribution coefficient of lead in this system over the ranges 1,350–1,650° C and 5–40 kbar is $K^{m/s} = 2.5 \pm 0.5$.

A relationship exists between the mean metal–silicate distribution coefficient for lead $K^{m/s}$ and the time interval ΔT_c between accretion of the Earth and segregation of the core. To calculate ΔT_c precisely, we need to know, in addition to $K^{m/s}$, (i) T_0, the age of accretion for the Earth; (ii) the isotopic composition of lead incorporated into the Earth at accretion; (iii) the isotopic composition of lead which has evolved in rock systems which have experienced no change in Pb/U (except as a result of radioactive decay) between the time of core formation and the time of emplacement in their present setting.

A detailed discussion of the relationship between $K^{m/s}$ and ΔT_c and of the boundary conditions (i), (ii) and (iii) is in preparation. For present purposes, a summary will suffice. For the age of accretion of the Earth, we take $T_0 = 4.55 \times 10^9$ yr. For (ii), we take the isotopic composition of lead from the troilite phase of iron meteorites[27] $(Pb^{206}/Pb^{204})T_0 = 9.346$ and $(Pb^{207}/Pb^{204})T_0 = 10.218$. Finally, for (iii) we chose the isotopic composition of lead from young oceanic tholeiites dredged from the floor of the Pacific Ocean[28]. Using these boundary conditions the relation between $K^{m/s}$ and ΔT_c is shown in Fig. 1.

The model with a metal phase composition $Fe_{83}S_{15}C_2$ approximates to a widely discussed class of hypotheses concerning the composition and origin of the Earth (accretion from mixed meteoritic material). The distribution coefficient for this composition is 2.5 and Fig. 1 shows that core segregation must have occurred within about 20 m.y. after accretion. For the $Fe_{70}S_{30}$ and $Fe_{89}Si_{11}$ compositions, $K^{m/s}$ values are larger; however, because the ΔT_c curve is very steep above $K = 1.5$, the ΔT_c intervals are only slightly shorter. We conclude that the Earth's core formed either during accretion of the Earth or very soon after. Variations in the boundary condition parameters (i), (ii) and (iii) within reasonable and acceptable limits do not affect this basic conclusion. The upper limit to ΔT_c for reasonable sets of boundary conditions is about 2×10^8 yr for $K^{m/s} = 2.5$, as measured.

The only significant uncertainty in these results is the possibility of a substantial negative pressure coefficient of $K^{m/s}$. Our results for the pressure range 0–40 kbar show that a large pressure coefficient does not exist. The scatter in the results could, however, conceal a relatively small positive or negative pressure coefficient. A pressure of 40 kbar is roughly one-tenth of the median pressure in the mantle so that the experimental pressure range over which distribution coefficients were measured is not insignificant. Moreover, plausible theories of core formation[8,22] involve equilibration of metal and silicate at relatively low pressures in the upper mantle, followed by segregation of metal into large drops which sink to the centre rather rapidly without altering the equilibrium which was established at low pressure. Nevertheless, we plan to extend these measurements to 100 kbar. Quite a large negative coefficient would be necessary to reduce $K^{m/s}$ to 0.4 at 400 kbar. As can be seen from Fig. 1, even with this value core formation must occur in less than 100 m.y. For FeSi and FeS cores, the corresponding time intervals would be much shorter.

We conclude that the time interval ΔT_c between accretion of the Earth and formation of the core was relatively short. Most probably, ΔT_c was smaller than 10^8 yr and almost certainly it was smaller than 5×10^8 yr. Core formation could well have occurred simultaneously with accretion. This constitutes a fundamental boundary condition for theories of the Earth's origin, and strongly favours models in which much of the accretion of the Earth occurred under sustained high temperature conditions[8-11]. Conversely, models of the type which have prevailed for two decades[1-7,20-22] and which regard the Earth as having accreted in a cool, unmelted state, followed by subsequent internal heating supported by long lived radioactivities, ultimately culminating in core formation at a much later stage, no longer appear tenable.

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Solidity of the Inner Core of the Earth inferred from Normal Mode Observations

SOLIDITY of the inner core was originally inferred on the basis of the assumption that the inner core has the same composition as the surrounding material of the outer core[1]. If, however, the observed increase in compressional velocity is related to a compositional change or, as suggested by Elsasser and Isenberg[2], to a new phase of iron with rearranged electronic orbits, then the inner core might be liquid[3]. It was believed that conclusive evidence of solidity of the inner core would come from observations of body waves of the type PKJKP, SKJKS or SKJKP, phases that travel through the inner core as a shear wave. But no reliable observations of these phases have been reported so far.

Here we present evidence for solidity of the inner core based on observations of normal modes reported by Dziewonski and Gilbert[4]. The pertinent modes and observed values of their periods are listed in Table 1. With the exception of ${}_2S_2$ all these modes were either misidentified or remained unidentified in Table 5 of Derr[5]. Recently Dratler *et al.*[6] gave the correct identifications of ${}_2S_0$ and ${}_4S_0$.

Dziewonski[7] inferred from observations of radial overtones ${}_1S_0$, ${}_2S_0$ and ${}_3S_0$ that introduction of a solid inner core represents the simplest explanation of the observed periods of these modes. The additional evidence gathered since that publication led to a revised model UTD124B′ with a value of 3.517 km s^{-1} for the average shear velocity in the inner core[4]. The theoretical periods computed for this model are shown in Table 1. The r.m.s. error of the residuals for all nine modes is 0.12%.

Dziewonski and Gilbert[4] calculated the energy balance for each mode following the method of Backus and Gilbert[8]. Table 1 shows the compressional and shear energies in the inner core presented as fractions of the total potential energy. The modes in Table 1 can be divided into two groups according to the predominant type of energy. Group 1 consists of modes with mostly compressional energy (${}_1S_0$, ${}_2S_0$, ${}_3S_0$, ${}_4S_0$, ${}_6S_1$, ${}_8S_1$), and the modes with predominantly shear energy belong to group 2 (${}_2S_2$, ${}_5S_2$, ${}_7S_3$); the energy of the mode ${}_8S_1$ is distributed rather evenly.

Although the rigidity of the inner core introduces relatively large non-linear effects, equation (49) of Backus and Gilbert[8] should predict the correct sign of the change in frequency due to variations of elastic parameters for modes with strongly polarized energy. A decrease in rigidity will increase the bulk modulus and consequently increase the frequency of the modes of group 1, and at the same time decrease the frequency of the modes of group 2 with predominantly shear energy.

To test the correctness of this estimate we have introduced a liquid inner core in the model UTD124B′, retaining all the other parameters unaltered. The results of calculations shown in Table 1 confirm in all cases the predicted change in the eigenfrequency. Of all the other modes identified by Dziewonski and Gilbert[4] only ${}_0S_2$ and ${}_2S_3$ show a 0.2% change due to the modification in the model, and for all remaining modes the change is less than 0.1%. Observations of these modes can therefore be considered irrelevant to the question of the solid against liquid inner core.

The r.m.s. error for the nine modes is practically the same for the three liquid inner core models: modified UTD124B′, 5.08M[9] and HB_1[10] (all of which satisfy the travel time data rather well), and it is more than eight times greater than for model UTD12B′. Also, the sign of the residuals for the individual modes is the same in all cases. This implies that the agreement between the observed data and eigenfrequencies computed for models 5.08M and HB_1 could be significantly improved by the introduction of rigidity in the inner core of these models.

Our argument has shown so far that there is no doubt that solidity of the inner core represents a simple and logical "data consistent" answer. The important question is whether it is a

Table 1 Observed Normal Modes of the Earth sensitive to the Structure of the Inner Core

				UTD124B′—Solid inner core				UTD124B′—Liquid inner core		5.08M		HB_1	
						Inner core energy							
Mode	Mean period (s)	No. of observations	s.e.m. (s)	Comp. period	Rel. error (%)	Compr.	Shear	Comp. period	Rel. error (%)	Comp. period	Rel. error (%)	Comp. period	Rel. error (%)
${}_1S_0$	613.57	11	0.236	614.59	0.17	0.181	0.000	607.39	−1.02	610.06	−0.57	607.4	−1.01
${}_2S_0$	398.54	40	0.084	397.59	−0.24	0.206	0.001	392.31	−1.59	391.42	−1.81	394.0	−1.14
${}_3S_0$	305.84	7	0.129	306.00	0.05	0.233	0.003	301.36	−1.48	301.84	−1.31	300.9	−1.62
${}_4S_0$	243.59	12	0.067	243.80	0.09	0.192	0.007	241.11	−1.03	241.55	−0.84	239.9	−1.51
${}_2S_2$	904.23	21	0.487	904.43	0.02	0.001	0.080	914.94	1.17	917.80	1.50	915.1	1.20
${}_5S_2$	397.36	11	0.157	397.03	−0.09	0.015	0.102	399.93	0.67	398.20	0.21	399.1	0.44
${}_6S_1$	348.41	21	0.046	348.23	−0.05	0.068	0.011	347.10	−0.38	347.38	−0.30	346.6	−0.52
${}_7S_3$	281.37	11	0.113	281.59	0.08	0.004	0.022	282.77	0.50	283.34	0.70	282.1	0.22
${}_8S_1$	272.10	11	0.144	271.79	−0.11	0.115	0.052	271.00	−0.40	270.92	−0.43	270.5	−0.59
	Nine modes—r.m.s.				0.12				1.01		1.00		1.02

unique answer, that is, whether it is possible to construct a model with a liquid inner core which would satisfy all the observations.

The attempts to match the data for the modes belonging to group 1 with a liquid inner core model invariably result in a decrease of density in the inner core below the outer core value at the inner–outer core boundary. This result could have been expected, for with relatively well established values for the compressional velocity and zero rigidity the only other way to reduce the bulk modulus is to decrease the density. A reversal of density in this region of the Earth's interior represents an implausible solution. It might be possible to match group 1 data without a density reversal by introducing a strongly super-adiabatic density gradient in the lower outer core to distribute the required decrease in the bulk modulus over a larger volume. But the data of group 2 would remain unsatisfied, and their residuals would in fact increase.

Because the modes of group 2 would have zero energy in the inner core if it were liquid, the only way to increase their eigenfrequencies would be to increase the bulk modulus in the outer core, a condition contradicting that necessary to satisfy the data of group 1. We therefore conclude that solidity of the inner core represents the only solution consistent with the observations of normal modes.

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BIOLOGICAL SCIENCES

Ligandin: a Hepatic Protein which Binds Steroids, Bilirubin, Carcinogens and a Number of Exogenous Organic Anions

THREE protein preparations from the rat liver 100,000*g* supernatant fraction have been independently purified to homogeneity. They are basic azodye carcinogen-binding protein (β-ABP)[1,2], corticosteroid Binder I[3,4] and Y protein[5]. The compounds they bind include certain steroids and their metabolites, bilirubin and certain carcinogens and their metabolites. Several dyes and cholecystographic agents and other organic anions are also bound (Table 1). Binding occurs whether the compounds are injected *in vivo* or added *in vitro* to liver homogenates.

We now present strong evidence to show that these three proteins are identical. For example, a comparison of their physical and chemical properties shows a close similarity[6,7] (Table 2). Furthermore, preparations of β-ABP bind bilirubin, bromsulphphthalein and 2-hydroxyoestradiol-glutathione conjugate. Immunochemical experiments give further support for identity. Monospecific antibodies to Y protein and Binder I show identity between Y protein, Binder I and β-ABP[8]. Similarly, monospecific antibodies prepared against β-ABP[9] show a similar identity among these three proteins. We have concluded that we are dealing with the same protein and because of its binding properties have decided to call it "ligandin".

Table 1 Compounds Bound by Ligandin

Compound	Laboratory	Nature of binding
Azodye carcinogen	(K) (L)	Covalent[1,6]
Azodye-GSH conjugate	(K)	Noncovalent[6]
Corticosteroids	(L)	Noncovalent[9]
Corticosteroid anionic metabolites	(L)	Noncovalent[3,4]
Oestradiol metabolites	(L) (K)	Noncovalent[9]
Bilirubin	(A) (K)	Noncovalent[5,8,17–19]
Bromsulphphthalein	(A) (K)	Noncovalent[5,8,10–12,14,17–19]
Indocyanine green	(A)	Noncovalent[5,19]
Phylloerythrin	(A)	Noncovalent[5,11]
Iodopanoic acid	(A)	Noncovalent[5,11]
Flavaspidic acid	(A)	Noncovalent[5,11]
Methylcholanthrene	(L)	Noncovalent[16]
Methylcholanthrene metabolite	(L)	Covalent[16]

K, Ketterer; L, Litwack; A, Arias.

Table 2 Physical and Chemical Properties of Ligandin

$S_{20,w}$	3.5 (K), 3.47 (L), 3.5 (A)
$S^{\circ}_{20,w}$	3.7 (L)
Molecular weight	
(*a*) Protomer	
Gel filtration	45,000 (K), 44,000 (A), 37,800 (L)
Sedimentation-diffusion	36,000 (L)
Sedimentation-equilibrium	45,900 (K), 42,900 (A)
Amino-acid analysis	37,300 (L)
(*b*) Subunits	23,000 (K), 22,000 (A)
pH_I (boundary electrophoresis) (isoelectrofocusing)	8.4 (K), 8.7 (A) 8.9 (L), ~9.0 (K), 8.7 (A)
Amino-acid analysis (approximate)	Asp_{34}, Thr_{11}, Ser_{13}, Glu_{39}, Pro_{16} Gly_{18}, Ala_{26}, Val_{17}, Met_{14}, Leu_{46} $Ileu_{19}$, Tyr_{12}, Phe_{17}, Lys_{33}, His_5 His_5, Arg_{21}, Try_2, Cys_4 (Similar analyses found by all authors)

K, Ketterer; L, Litwack; A, Arias.

Ligandin is abundant in rat liver and immunochemical titration in one laboratory gave it a value of 4.46% of the total cell sap protein[8] and, in another, a value of 4%. From binding studies, it also seems to be present in fully developed amphibia, reptiles, birds and mammals including monkey and man, but is absent from gill-breathing vertebrates[10–12,14]. Its levels are low in the foetal liver, but increase rapidly *post-partum*[10–14], and are also low in hepatomas[13,15,16].

Although most abundant in the liver, ligandin has also been identified in the kidney[8,15], where it occurs in the tubule cells[8] and also in mucosal cells of the small intestine[8]. Ligandin constitutes approximately 2% of supernatant protein in homogenates of kidney and small intestinal mucosa and has not been detected in plasma, bile, brain or other tissues[8].

Ligandin binds a range of endogenous substances noncovalently but the affinity of binding varies. For example, oestradiol metabolites seem to bind with equal or greater affinity than corticosteroid metabolites[9], and bromsulphthalein can be displaced by low concentrations of bilirubin but not by bile salts[5]. There is also specificity of binding among carcinogens. For example, whereas azodye carcinogens[1,2,6] and methylcholanthrene[16] are bound, acetylaminofluorene, a carcinogen with which azodye carcinogens are often compared biochemically, is not bound.

Carcinogens differ from other compounds in that in addition to binding to ligandin noncovalently, they also bind covalently. For example, azodye carcinogens are bound noncovalently as a glutathione conjugate[6] and are also bound covalently to the protein through the sulphur of a cysteinyl residue[17]. Methylcholanthrene also binds both noncovalently and covalently[16].

Compounds which induce drug and steroid metabolizing enzymes of the endoplasmic reticulum (for example, phenobarbitone and DDT) also induce ligandin[8,18-20].

In ontogenetic, phylogenetic, induction and competition experiments, there is a direct relationship between the hepatic concentration of ligandin and the net flux of bilirubin, bromsulphthalein and other organic anions between plasma and the liver cell[5,8,10-12,14,18-20]. These observations support the hypothesis that ligandin is a major determinant of selective hepatic uptake of certain small molecules and may also influence the flux of metabolites from the liver into the plasma or bile.

Where steroids and carcinogens are concerned, however, azodye-binding protein has been detected in the nucleoplasm[21] and an additional function of ligandin may be to transport compounds which affect cellular differentiation into the nucleus.

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Human Repetitious DNA, Satellite DNA and Chromosome Interarm Fibres

IT is of interest that RNA (cRNA) made complementary *in vitro* to human repetitious DNA has been found to hybridize with human chromosomal DNA at the centromeres and at the ends of the arms in light microscope cytological preparations[1]. These are the locations where we saw the largest number of DNA-containing interarm fibres in electron micrographs of whole mount human mitotic chromosomes[2] (Fig. 1).

Previously, mouse satellite DNA, a highly repetitious fraction of mouse DNA[3], was also found to be localized at the centromeres in mouse chromosomes hybridized with mouse satellite cRNA[4,5]. The similarities in chromosome localization and the repetitive nature make the human repetitious DNA found by Arrighi *et al.*[1] a likely candidate for human satellite DNA.

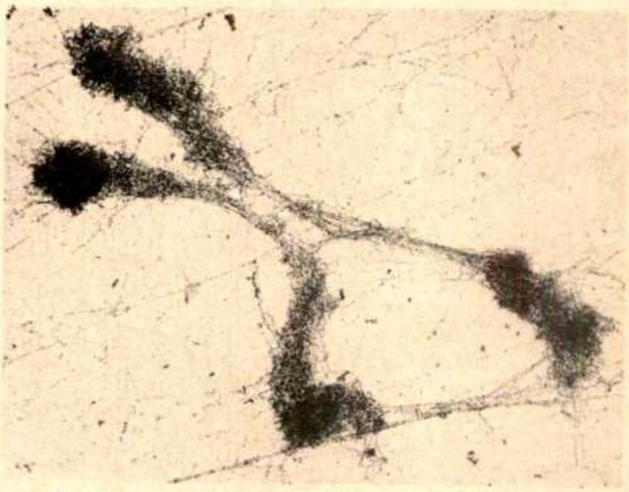

Fig. 1 A human lymphocyte chromosome treated with 25 µg/ml. trypsin (Worthington) showing fibre attachments at the centromere and bottom arms (× 6,125).

In addition to interarm fibres crossing at the centromere and at the ends of arms in human chromosomes, we found fibres crossing all along the length of the sister chromatids in some chromosomes (Fig. 2). These fibres were fewer in number at their crossing sites. The fact that they were not always seen may have been due to the stretching forces exerted on the chromosomes when they were placed on the water surface of a Langmuir trough before being picked up on electron microscope grids. The only interarm fibres which were always seen were those crossing at the centromere.

The interarm fibres found at sites other than the centromere and ends of arms would also have been expected to hybridize with cRNA to repetitious DNA if they contain repetitious DNA. One reason for this apparent contradiction may be that the DNA template for the complementary RNA did not contain all sequences for the repetitious DNA. Corneo *et al.*[6] have isolated a second human satellite DNA fraction. Another reason for the apparent lack of hybridization might be the smaller number of fibres and therefore fewer genes involved at these sites. In *Drosophila* salivary gland chromosomes which contain multiple copies of genes Hennig *et al.*[7] found *Drosophila* satellite DNA in some species distributed all along the chromosome bands, although predominantly located at the kinetochore. They noted that the gene enhancement of polytene chromosomes may have increased the possibility of detecting satellite DNA at sites not detectable in normal chromosomes.

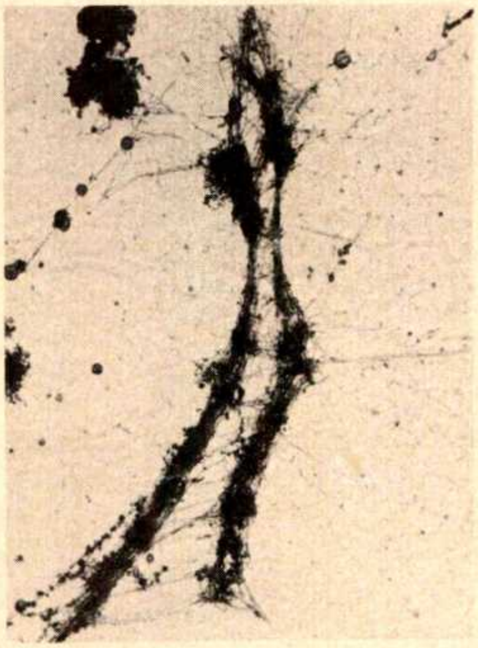

Fig. 2 Relaxation of chromosome with 800 μg/ml. pronase to reveal many interarm fibres crossing all along the length of the two chromatids (×9,100). (Reproduced by permission of the editor of *J. Cell Biol.*)

Satellite DNA seems to be different from total chromosomal DNA in many ways. First, it bands at a different buoyant density in caesium chloride gradients, showing a different base composition[8,9]. Second, it is highly repetitious and reassociates rapidly after denaturation[10]. Third, it does not seem to code for protein in the mouse, or, as in the case of guinea-pig a satellite, to code for an aberrant protein[11]. Fourth, Maio and Schildkraut found mouse satellite DNA to be associated with different protein components after extraction of isolated mouse chromosomes with high salt[12]. Fifth, it has been found in association with constitutive heterochromatin in mouse cells[13]. Sixth, it has the apparently discrete chromosome localization when hybridized with complementary RNA.

What is a possible role for interarm fibre-satellite DNA? Does it challenge the classic genetic theory of a complete set of chromosomal genes within each chromatid to find genome-carrying fibres running between sister chromatids? If highly repetitious DNA does not code for protein, it may have the structural role proposed by Walker *et al.*[3]. And that role may be to package genome DNA for delivery to daughter cells.

The mechanism which causes the separation or dissolution of the interarm fibres at cell division remains unknown. Failure of the fibres to separate, however, might cause the two chromatids to be drawn into the same daughter cell. This might result in the phenomenon, trisomy, where three homologous chromosomes instead of two are found at the next metaphase.

The electron microscopy of chromosomes was done at the Bureau of Radiological Health, Division of Biological Effects, Rockville, Maryland 20852.

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Changes in Biological Conditions in the English Channel off Plymouth during the Last Half Century

COMPARABLE observations on chemical and biological conditions in the western English Channel off Plymouth have been made with varying regularity and intensity since 1921, and regular records of nutrient salts and the larger zooplankton were kept from 1924 to 1939. During that period a notable change took place: the herring fishery, which had been a regular winter feature at Plymouth, petered out in the early 1930s when young herring ceased to join the shoals[1,2], and at the same time there was a decrease in the amount of nutrient salts present in the water in the winter[3] and a very marked decline in the quantity of zooplankton including the planktonic stages of bottom-living fish. From 1935 pilchard seemed to take the place of herring[4].

After the Second World War observations were resumed, and since 1965 there has been a return to the conditions which were familiar in the 1920s[5,6]. Evidence from a number of sources confirms these changes, including observations on nutrient salts, primary productivity, phytoplankton succession and zooplankton abundance, and numbers of young and adult fish. A general summary of some of the events is shown graphically in Fig. 1.

One of the more striking features of the earlier period was the decrease in the maximum winter phosphate values, which fell from an average of 0.67 μg/at. P/l. during 1924–29 to an average of 0.48 during 1931–38. Analyses have been continued regularly[7,8] apart from the war years and tests have been made to ensure that the results are strictly comparable in spite of changes in methods. In general the low winter phosphate levels prevailed, although three isolated years did show higher values than in 1931–38 (similar annual fluctuations also appear in the period of high winter phosphate levels). Since 1969, however, we have had two consecutive years of high

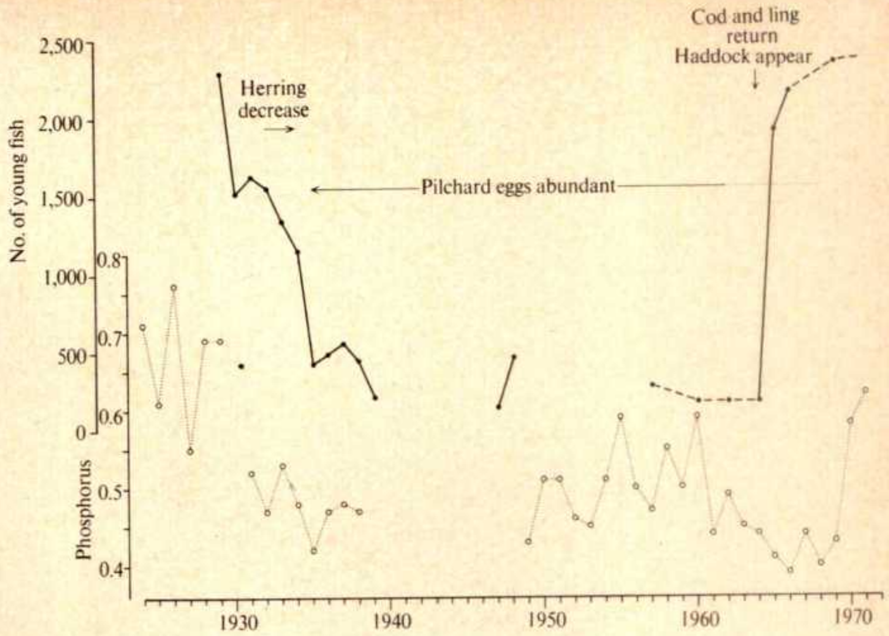

Fig. 1 Diagram to show (*a*) sums of average monthly catches of young fish (excluding clupeids) in standard hauls of the 2 m ring trawl off Plymouth (●—●), 1924–29 being shown as the average for those years; (*b*) winter maxima of inorganic phosphate (○···○) as μg/at. P/l. Changes in occurrence of herring, pilchard and certain gadoids are also given.

winter phosphate, the value of 0.62 found in 1971 being the highest recorded since the "rich" years before 1930, and not far removed from the average for that period.

Measurements of primary production by the ^{14}C method have been made since 1964. Assessments of total annual production in grams of carbon under 1 m^2 sea surface show an increase in recent years as follows: 1965, 140; 1966, 166; 1967, 127; 1968, 188; 1969, 195; 1970, 212.

At the same time there has been a steady increase in the spring maximum of phytoplankton since 1967. The diatoms *Biddulphia sinensis* and *Coscinodiscus concinnus* have also become much more abundant in the spring and early summer during the past 4 or 5 yr.

Until 1931 regular zooplankton collections made with the 2 m net (ringtrawl) had been very rich in numbers of animals especially the copepod *Calanus* and larval stages of Crustacea[9]. The samples were also characterized by the occurrence of certain species of medusae, larval worms, echinoderm larvae and euphausids which disappeared almost completely during the late 1930s. After 1935, however, there was a notable increase in the numbers of eggs and post-larvae of pilchard, especially from April to July. When sampling was resumed in 1945 it was clear that the conditions found in 1935–39 still prevailed. Although the methods had to be modified slightly after the war and although collections were not made so regularly in certain years, a watch was kept on the situation, and a careful series of comparisons was made of the sampling capacity of the nets to ensure continuity of the series. In about 1965 it was evident that a change was taking place, and since then observations have been intensified. The numbers of the planktonic stages of teleostean fish other than clupeids increased spectacularly and have returned in abundance approximating to that found in the "rich" years before 1930. By 1970 the whole catch of zooplankton had increased greatly; *Calanus* was once more extremely abundant in the late spring (Fig. 2), and other animals such as larval forms of worms and echinoderms and euphausids which had virtually disappeared in the 1930s became quite frequent again in the catches. Coincident with these changes in young fish and zooplankton there are indications of a reduction in the intensity of spawning of pilchard and a shift of the main season of abundance of pilchard eggs away from the spring and early summer months towards the autumn. There are also some signs that herring may be returning to the area, although not yet in sufficient numbers to support a fishery.

These changes seem to be linked in some way. Plymouth lies close to a well marked boundary between boreal forms and warm water species. Thus the years of paucity of plankton and abundance of pilchard may correspond to a period of general retreat northward of the boreal fauna during the recent amelioration of climate in the northern hemisphere. That boreal forms are now returning during a period of worsening climate is borne out by the evidence for recent increases in numbers of adult fish such as cod and ling, while haddock have appeared for the first time. Additional evidence has been found on the seashore where boreal forms such as *Balanus balanoides* have increased greatly since 1961[10]. Much of the initial increase in the non-clupeid young fish which we noted in 1965–66 must

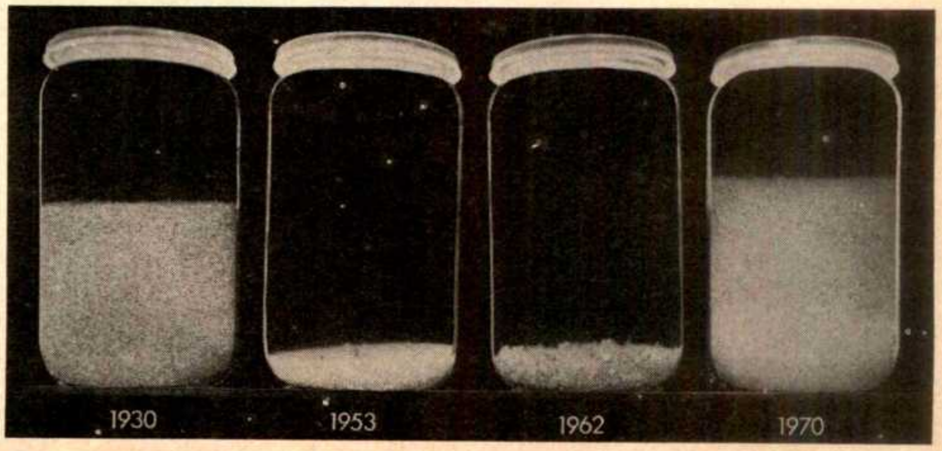

Fig. 2 The relative abundance of larger zooplankton off Plymouth in certain years, as sampled with the 2 m net (about 5,000 M^3 of water filtered in a standard haul). The catches are the maxima found each year in late May or June, and are shown settled in jars holding 2 l. The 1953 sample is almost entirely eggs of pilchard, while *Calanus* predominates in the 1930 and 1970 samples. (Photo by D. Nicholson.)

itself have been due to a local increase in the population of adult fish.

A number of theories have been put forward to explain the decrease in nutrient salts and plankton during the 1930s (summarized in ref. 11). Now that conditions are returning to the earlier state there seems little doubt that basically the cycle must be related to climatic change. Warming of the Arctic would affect circulation in the North Sea by allowing Atlantic water to extend farther north, thus reducing the pressure from the north and from the south-west (through the English Channel)[12]. Cooling will have the reverse effect and intensify penetration into the North Sea from these directions. At the same time the population centres of northern fish and plankton animals will shift towards the south again.

The whole picture thus results from a combination of factors, namely climatic change, its effects on water movements, and shifting of centres of animal populations. The resulting changes in the ecosystem may also affect the cycle of nutrients[4]. More detailed accounts of different aspects of this research will be published elsewhere.

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Evidence for a Conformational Change in Nerve Membrane with Depolarization

THERE has been much interest in identifying and characterizing the protein elements in cell membranes which seem to be involved in regulating membrane ionic permeability[1-3]. We now have further evidence that membrane-bound proteins in nerve axons are involved in ion permeability regulation. It was first found that external treatment of isolated crayfish nerve axons with the proteolytic enzymes papain, trypsin, and chymotrypsin (unpublished data) considerably affected the axons, resting permeability to potassium, sodium, and chloride, while having minimal effects on the action potential. It was also found that the external application of 1-fluoro 2,4-dinitrobenzene (which reacts with protein reactive groups) considerably reduced chloride permeability without reducing the resting membrane potential or action potential[4].

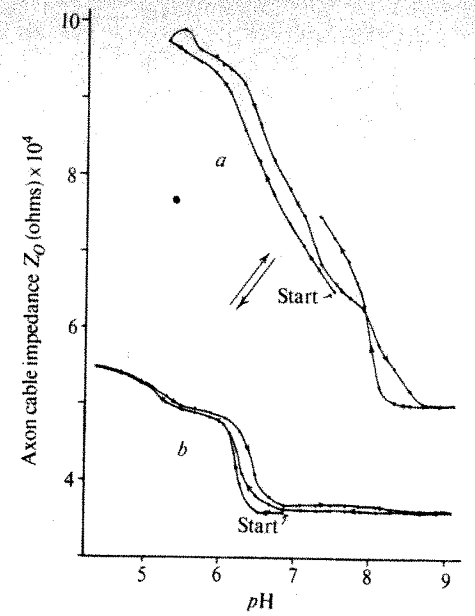

Fig. 2 Impedance of the axon. *a*, Resting axon, $K_0 = 5.4$ mM, $V_m = -87$ mV; *b*, potassium depolarized axon, $K_0 = 40$ mM, $V_m = -43$ mV.

Further information on the permeability role of membrane-bound protein was obtained by measuring the axon cable impedance Z_o as a function of *p*H, where $Z_o{}^2 = r_m(r_i + r_o)$. Changes due to *p*H in the axoplasmic resistance r_i and external resistance r_o would not be expected to occur, for these resistances primarily depend on the free ions potassium, sodium and chloride. Therefore, any change in the axon cable impedance Z_o with *p*H would primarily reflect those changes which occur in the membrane resistance r_m.

In the experiments described here, the medial giant axon from the ventral nerve cord of crayfish (*Procambarus clarkii*) was dissected from its adjacent axons in saline containing (mM): NaCl 205, KCl 5.4, $CaCl_2$ 13.5, $MgCl_2$ 2.6, Tris (hydroxymethyl) aminomethane-maleate buffer 5.0. The *p*H was adjusted by adding either HCl or NaOH to the saline. The axon was cannulated with a micro-pipette electrode through which constant current pulses ΔI were injected (Fig. 1). From the opposite end of the axon, a potential recording micro-pipette was also inserted to record the membrane potential V_m, and the change in membrane potential, ΔV_m, due to the injected constant current pulses. From these measurements, the axon cable impedance Z_o was determined as $2\Delta V_m/\Delta I$.

Titration of the axon revealed a *p*H dependency of the axon cable impedance which closely resembled a protein dissociation curve (Fig. 2*a*). Back titration from the *p*H extremes of 5 and 10 often resulted in hysteresis or completely new curves such as might indicate exposure of new ionizing groups as a result of denaturation. The results from axon to axon showed considerable variability in the absolute magnitude of cable impedance but the regions of impedance transition

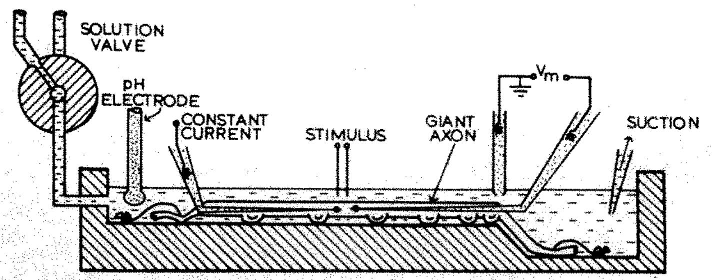

Fig. 1 The perfusion chamber.

with *p*H remained essentially unaltered. Most noticeable have been transitions in cable impedance around *p*H 6.3 and *p*H 8 to 8.5. These are tentatively identified as resulting from histidine and sulphydryl groups.

Experiments were also performed in elevated external potassium solution which depolarized the axon membrane more than enough to produce an action potential if this depolarization were done by voltage stimulating electrodes. This depolarization was also sufficient to produce "sodium inactivation" and render the axon inexcitable. In the potassium depolarized state, the axon cable impedance is less than that of the axon in normal saline and the cable impedance changes with *p*H show less overall variation (Fig. 2*b*). Less variation in the data from axon to axon in the depolarized state is obtained. An especially steep portion of the *p*H dependence curve occurs in the *p*H range 6 to 6.5. We believe this represents a cooperative transition in the surface membrane protein. This transition probably involves the unmasking of buried histidine residues. The data here suggest that the process of nerve excitation involves a change in the conformation of membrane-bound protein where an increase in the potassium ion concentration in the membrane displaces calcium during depolarization. This potassium-calcium displacement mechanism has often been suggested as a possible mechanism for nerve excitation[5].

Further evidence here that histidine is involved in excitation comes from photo-oxidation studies utilizing rose Bengal[6], which, when used to treat the axons, resulted in immediate loss of the action potential and a slower loss of membrane potential on exposure to light. This effect was mitigated when the amount of magnesium present was increased. These results strengthen our view that a conformational transition involving histidine groups of surface membrane proteins is involved in the action potential and an ion permeability regulation.

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X-ray-induced Morphological Differentiation of Mouse Neuroblastoma Cells *in vitro*

THE high radiosensitivity of undifferentiated human neuroblastoma is well known, but the nature of changes induced by irradiation is uncertain. Two ideas have emerged from the observations of radiobiologists and radiotherapists: (*a*) neuroblastoma cells are destroyed or (*b*) they are induced to differentiate or "mature" into ganglioneuroma by ionizing radiation. Experimental evidence to support the hypothesis of radiation-induced differentiation is lacking. The availability of mouse neuroblastoma cell culture provides an opportunity to study the nature of cellular alterations produced by ionizing radiation. This paper shows that X-irradiation induced morphological differentiation of neuroblastoma cells which in the presence of serum undergo morphological maturation.

In our laboratory, neuroblastoma cells have been cultured from the primary mouse tumour by the procedure of Dr R. Klebe, of Yale University. Cells have not been cloned. They are grown as a monolayer in the Falcon plastic flask containing F12 medium with 10% agamma globulin newborn calf serum, penicillin (100 μg/ml.) and streptomycin (100 U/ml.) and are maintained at 36° C in a humidified atmosphere of 5% CO_2 in air. When grown in Falcon plastic flasks, the average doubling time of neuroblastoma cells is 24 h. This cell line has acetylcholinesterase but no butyrylcholinesterase activity, indicating its neuronal nature[1]. Cells (10^5) were plated in a T-30 flask and X-irradiated 24 h later. Radiation factors were 250 kVp, 30 mA, with added filtration 0.5 mm Cu and 1.0 mm Al (hvt = 1.36 mm Cu). Dose rate was 139 rad/min. The turntable was rotating during exposure. Cells were X-irradiated at room temperature with a single dose (200–1,000 rad) or a fractionated dose (800–1,400 rad, 200 rad/day). The medium in the irradiated cell population turned acidic relatively fast and therefore a frequent change of medium was necessary. For the study of the repair of irradiated neuroblastoma cells, the culture received 400 rad in two fractionated doses. The time interval between two fractions was 4 and 24 h. The irradiated controls received 400 rad in a single dose. The control cells were treated similarly except that no radiation was given.

The formation of axons (cytoplasmic extensions greater than 50 μm long) was regarded as an expression of morphological differentiation, and the enlargement of the nucleus and cell size as indicating morphological maturation. A single-cell suspension of control and irradiated cell population using 0.25% viokase solution for 20 min was prepared and the cells were counted with a haematocytometer. The cells stained with trypan blue (0.1% in saline) were considered dead and subtracted from the total count. The growth inhibition of the neuroblastoma cell population *in vitro* 3 days after irradiation was calculated as follows:

$$\frac{\text{No. of control cells} - \text{No. of irradiated cells}}{\text{No. of control cells}} \times 100$$

The cell viability was also determined after staining the attached cells with trypan blue.

X-irradiation of mouse neuroblastoma cell culture induced axon formation (Fig. 1*B*, *C*, and *D*) as well as enlargement of cellular and nuclear size. A similar change in cellular morphology is known to occur during development of the mammalian nervous system. There were several multinucleated differen-

Table 1 X-ray-induced Morphological Differentiation of Neuroblastoma Cells *in vitro*

Dose	Differentiated cells (% of total cell population) Days after treatment 1	2	3	4	% viability
Control	8 ± 1.5*	9 ± 2.5	12 ± 3.0	11 ± 1.6	95 ± 2.0
200 rad	—	—	17 ± 0.9	—	93 ± 2.0
400 rad	—	—	26 ± 3.5	—	83 ± 3.5
600 rad	22 ± 3.9	28 ± 5.9	39 ± 7.7	47 ± 3.4	67 ± 7.0
800 rad	—	—	40 ± 3.5	—	60 ± 6.0
800 rad (200 rad/day)	—	—	29 ± 2.0	—	81 ± 2.7
1,000 rad (200 rad/day)	—	—	27 ± 4.2	—	82 ± 2.7
1,200 rad (200 rad/day)	—	—	30 ± 0.9	—	69 ± 3.5

* Standard deviation.

Cytoplasmic extension greater than 50 μm in length was considered as an axon. Differentiated cells in the fractionated-dose experiment were counted one day after the last fractionated dose. The viability of cells was determined by using supravital stain (trypan blue). The stained cells were considered dead. Attached cells in the dish were first stained with trypan blue and then differentiated cells were scored to avoid the scoring of dead cells while counting the differentiated ones. The % viability was determined 3 days after single dose or 1 day after the last fractionated dose. Each value represents an average of six to ten samples.

tiated cells. The presence of polyploid neurones in the irradiated cell population has recently been confirmed by a higher DNA content per cell[1]. It is interesting to note that some mammalian neurones, such as Purkinje cells, are polyploids. Many irradiated cells increased in cellular and nuclear size without forming axons. The degenerative changes in the X-ray-induced differentiated cells were characterized by the appearance of vacuolated cytoplasms (Fig. 1*D*) and finally fragmentation of nuclear and cytoplasmic materials (Fig. 1*E*). These cellular changes resemble those observed when matured mammalian neurones are cultured in the absence of nerve growth factors. Almost all cells stained with trypan blue were smaller, indicating that all large cells in the irradiated cell population were viable.

Table 1 shows a quantitative evaluation of differentiated cells as a function of time and dose. The control cell population contained about 8% differentiated cells, whereas the irradiated cell population 24 h after 600 rad contained about 22% differentiated cells. At this time there was no significant cell loss in the irradiated cell population, so that the increase in the differentiated cell population cannot be attributed to the killing of radio-sensitive cells. The maximum increase in the differentiated cell population was seen 3–4 days after irradiation. The number of differentiated cells after a single dose appeared greater than that after a fractionated dose, indicating that dose was more important than the time (Table 1).

X-irradiation of Chinese hamster ovary (CHO) and baby hamster kidney-21 (BHK) cells *in vitro* did not produce morphological changes similar to those of neuroblastoma. CHO and BHK-21 cells were grown in experimental conditions similar to those of neuroblastoma cells.

Morphological maturation was evident as early as 24 h after irradiation, and by the third day most differentiated cells had matured morphologically. In the control cell population only a few of the differentiated cells matured morphologically. Did maturation of cells result from cellular changes produced by X-irradiation or from some "factor" in the serum? To investigate this question, serum-free medium was added immediately after X-irradiation (600 rad). Serum-free medium was also added to a non-irradiated cell population. Many cells in the irradiated and non-irradiated cell population formed relatively shorter axons, but the cellular and nuclear size did not increase. This showed that the presence of serum after X-irradiation was necessary for the expression of maturation. The formation of axon in the non-irradiated neuroblastoma cell population is consistent with an earlier observation[2]. Because of the induction of axons by serum-free medium, we wondered if the X-irradiation of the medium was changing the constituents of the serum in a way that induced differentiation. To investigate this, cells were X-irradiated (600 rad) and fresh growth medium was replaced immediately after exposure. In the irradiated controls, growth medium was not changed. The

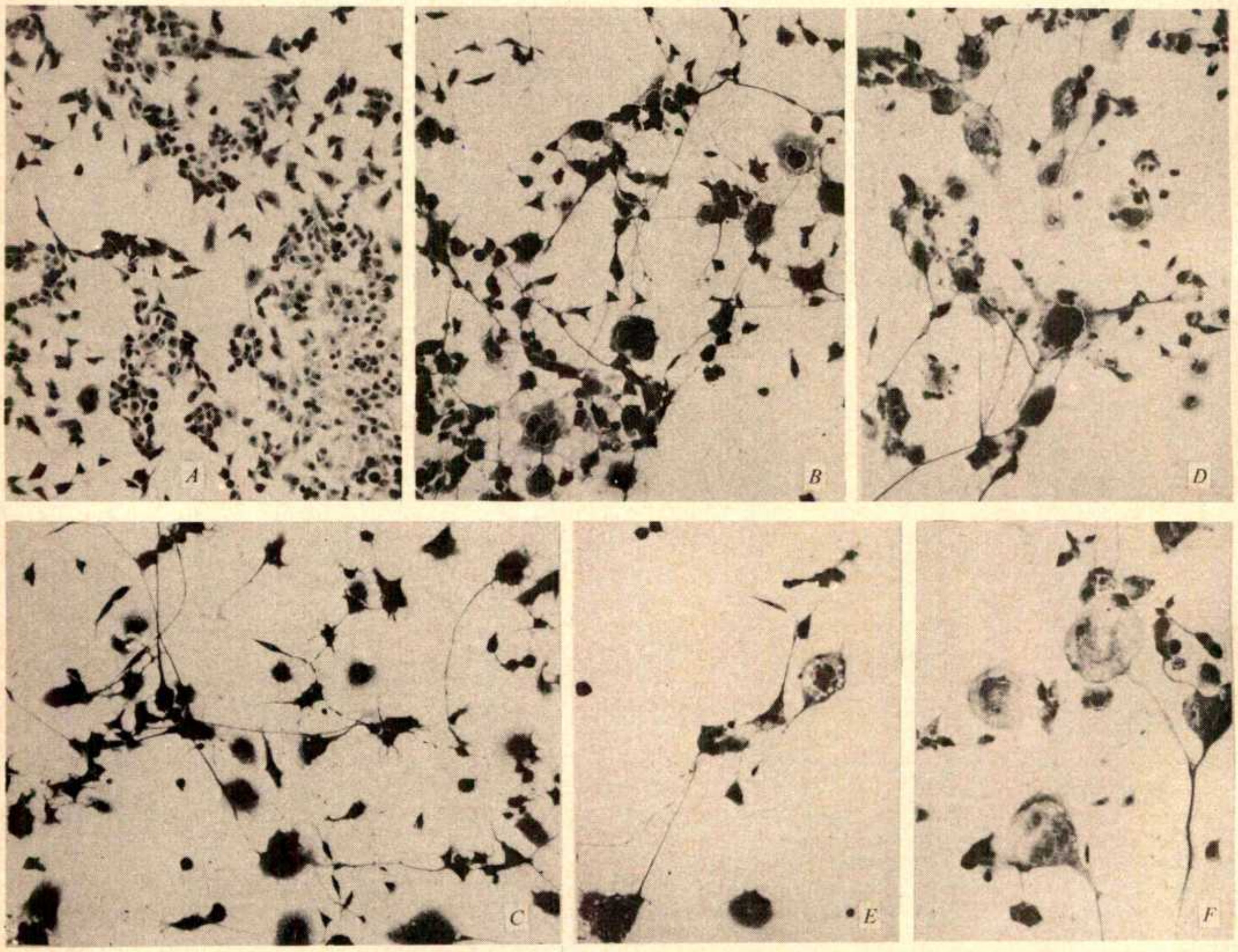

Fig. 1 Photomicrographs of control and irradiated cell population. Cells while attached to the flask were fixed in formaldehyde (1 : 10 dilution of concentrated formaldehyde) for 20–30 s, washed quickly once with distilled water, stained with 0.1% cresyl violet for 2 min, rinsed quickly twice with distilled water and air-dried. Immersion oil (3 ml.) was added to the flask before taking photomicrographs. Non-irradiated cell population (*A*) showed small, round and undifferentiated cells. Irradiated cell population (*B*) and (*C*) received a single dose of 600 rad and 1,000 rad respectively. Many differentiated and matured cells were present 4 days after irradiation. The irradiated cell population (*D*) was given 1,400 rad (200 rad/day) and stained 24 h after the last dose. Vacuolated cytoplasm (*E*) and fragmentation of cytoplasmic and nuclear materials (*F*) in matured neurones were also observed (× 56).

differentiation and maturation in both groups of irradiated cell population occurred in a similar manner. A change in serum constituents was therefore not responsible for the radiation-induced morphological differentiation.

Table 2 Effect of X-irradiation on Mouse Neuroblastoma Cells *in vitro*

Dose (rad)	% inhibition	(Total number of cells × 10^4)
Control	0	106.0 ± 6.0
200	27.0 ± 4.0*	81.0 ± 8.0
400	62.0 ± 2.0	41.0 ± 4.6
600	80.0 ± 1.0	21.7 ± 0.4
800	92.0 ± 2.0	9.9 ± 1.5
1,000	94.0 ± 1.0	6.6 ± 0.7
200 + 0 h + 200	66.0 ± 4.0	37.0 ± 6.0
200 + 4 h + 200	50.0 ± 4.0	54.0 ± 2.9
200 + 24 h + 200	50.0 ± 6.0	54.0 ± 3.7
1,200 (200 rad/day)†		35.0 ± 3.0

* Standard deviation.

† Cells were counted 1 day after the last dose.

Cells were X-irradiated 24 h after plating and counted 3 days after irradiation. In the experiments using fractionated dose schedule, the cell number was counted 3 days after first dose. The % growth inhibition of neuroblastoma cell population was calculated as follows:

$$\frac{\text{No. of control cells} - \text{No. of irradiated cells}}{\text{No. of control cells}} \times 100$$

Each value represented an average of six to eight samples.

To study the recovery of neuroblastoma cells, a fractionated-dose technique[3] was used. The recovery was measured on the basis of cell survival. An interval of 4 h between two fractionated doses allowed only slight recovery (Table 2). Increasing the interval produced no further recovery. Our present criteria of measuring recovery assume the resumption of cell division after recovery; but X-irradiation induces differentiation and differentiated neuroblastoma cells would not resume cell division. Thus even though radiation damage may have been fully repaired, this cannot be measured on these criteria.

Vinblastine sulphate, which is known to interfere with the assembly of microtubules, inhibits the induction of axon formation by serum-free medium[2], dibutyryl adenosine 3′ 5′ cyclic monophosphate[4] and 5-bromodeoxyuridine[5]. When vinblastine sulphate (2.43×10^{-9} M) was added to the neuroblastoma culture immediately after X-irradiation, examination of the cells 3 days later showed that in this case also axon formation was inhibited.

X-irradiation inhibited the growth of neuroblastoma cells and this effect was dose-dependent (Table 2). Radiation is known to inhibit cell division, and so one may argue that inhibition of cell division is mandatory for morphological differentiation. The fact that serum-free medium blocks cell multiplication and induces axon formation in neuroblastoma cells[2] tends to support this contention. We have recently found, however, that dopamine, 6-hydroxydopamine[6] or DL-glyceraldehyde (Sakamoto and K. N. P., in preparation) inhibits cell division but does not induce morphological differentiation. The inhibition of cell multiplication is therefore not sufficient for morphological differentiation.

From these results it seems not only that X-irradiation induces differentiation of neuroblastoma cells, but that it accelerates maturation of differentiated cells. Moreoever, acetylcholinesterase activity in cells induced to differentiate by X-irradiation increases by a factor of ten[1]. The effects of vinblastine sulphate on induction of differentiation suggest that the effect of X-irradiation may depend on its promoting the assembly of microtubules.

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Fertility Reduced in a Caged Native House Fly Strain by the Introduction of Strains bearing Heterozygous Chromosomal Translocations

GENETIC manipulation of insect pests[1] is an attractive method of control because of its specificity. The numerous possible types of manipulations fit into two categories: (1) the release of sterile insects that affect only the succeeding generation and (2) the release of partially sterile or fully fertile insects that carry inherited factors which will affect several subsequent generations. The first category includes sterile males[2], hybrid sterility and cytoplasmic incompatibility[3]. The second category includes chromosomal translocations, other gross chromosomal abnormalities, recessive lethal mutations, sex-limited lethal mutations, detrimental and conditional lethal mutations, and a combination of meiotic drive plus detrimental or lethal factors.

So far most genetic manipulations have been of the first sort, but studies of genetic manipulations in the second category are in progress and we have been studying chromosomal translocations in the house fly, *Musca domestica* L. Translocations, when heterozygous, reduce fertility because a regular proportion of the products of meiosis (eggs and sperm) are deficient for chromosomal parts required for life (viability). Larval and pupal mortality is also increased in some cases. Several investigators have discussed the use of chromosomal translocations for suppressing insect populations[4,5]. Using X-rays, we induced more than 300 chromosomal translocations in house flies and we analysed each strain for egg hatch (fertility), transmission of the translocation, and sex ratios of progeny. Table 1 shows the results of this analysis for three strains that had a low fertility when the heterozygous translocation-bearing males were outcrossed with appropriately marked non-translocation-bearing virgin females. This procedure was practical

Table 1 Egg Hatch, Transmission of the Translocation, and Sex Ratio of Progeny from Three Strains of House Flies bearing Chromosomal Translocations involving Three Chromosomes

Translocation	Hatch (%)	Progeny bearing translocation (%)	Males (%)
A*	33.5	53.2	52.8
B*	30.7	48.0	51.0
C†	27.3	72.0	72.0

* Reciprocal translocation between three autosomes.

† Reciprocal translocation between the *Y* chromosome and two autosomes.

Males bearing the translocation were crossed to appropriately marked, non-translocation-bearing females.

because no crossing over occurs in the male house fly[6]. Two involved the reciprocal translocation of three autosomes (translocations A and B) and one involved the reciprocal translocation of the *Y* chromosome and two autosomes (translocation C).

For the tests, translocation-bearing males or males plus females of individual strains were placed in laboratory cages at one or two ratios (9 : 1 or 4 : 1) with virgin wild type males and females so the reduction of fertility (fertility coefficient) of the resulting matings could be assessed. The fertilities of F_1, F_2, and F_3 sib crosses with or without the addition of further heterozygous translocation-bearing flies were also assessed and the accumulated fertility coefficients (fertility compared with controls) were determined. Equal numbers of females were maintained in test and control cages. Also equal numbers of test and control larvae were allowed to develop in the same volume of medium.

The fertility and accumulated fertility coefficients were determined in the following way (C. F. Curtis, personal communication). Controls = 100% fertility. The fertility coefficient of the treated population = % fertility of the treated population compared to controls in generation 1. The accumulated fertility coefficient of the treated population in generation 2 = % fertility of the treated population compared to controls × the fertility coefficient of the treated population in generation 1, and so on.

Table 2 shows the lowered fertility obtained in the tests based on the reduction in egg hatch and on larval and pupal mortality compared with control populations containing wild type flies. With translocations A and B, the fertility coefficient ranged from 10.3 to 21.6% of controls in the first cross and the accumulated fertility coefficient through as many as four generations ranged from 1.0 to 6.4%. With translocation C, the lowered fertility ranged from 42.0 to 45.8% in the first cross and the accumulated fertility coefficient through four generations was 34.5%. The translocations involving three autosomes were more efficient at reducing fertilities than was the translocation in which the *Y* chromosome and two autosomes were reciprocally translocated.

We emphasize that population control, not eradication, is the goal of our research. If the greatest reduction in fertility we obtained in one generation, 89.7%, were maintained, it should hold a fly population static throughout the season or cause it to decrease if the reproductive potential is less than ten times and density-dependent factors are not operating. Thus the number of flies released plus the decreasing number of wild flies combined could be smaller than the wild population, even with fairly effective insecticide control. Results such as these could be realized in the field, and control of insect pests might be achieved, or the method might enhance control in combination measures.

The tests reported here are at best only simulations of natural circumstances. Flies for release (bearing the translocation) had to be separated from the non-translocation-bearing progeny of appropriate genetic crosses, and while the methods are operable in the laboratory, refinements would have to be introduced into the system to make such methods practicable for massive field releases. Small field trials are possible using the methods reported here, however, and have been undertaken at three sites in Florida during 1969 and 1970. The results of these tests will be reported later.

One refinement of the system includes the release of insects bearing homozygous rather than heterozygous translocations[7]. This is especially important when the insect stage released is itself the pest. Homozygous strains can be reared without selection, so large numbers are more easily obtained. Also, the maximum reduction in fertility that can be achieved by the release of homozygous translocations (up to 75%) is realized when the translocation chromosomes are 1 : 1 with the normal homologues in a population. Thus, fully competitive insects need be released only in a 1 : 1 ratio with the native insects, but to obtain more than a 90% reduction in fertility each generation, several strains bearing different translocations in the homozygous form would need to be utilized. We have obtained three homozygous translocation-bearing strains of house flies in fifteen attempts. All three cases involve the simplest form of reciprocal chromosomal rearrangement which includes just two chromosomes. Such translocations in the heterozygous form do not yield the required reduction in fertility necessary to reduce house fly populations. We must obtain homozygous translocation strains where more chromosomes are involved in the rearrangement and thus a greater reduction in fertility is obtained. We have twenty such strains in the heterozygous form. The final requirement is that the strains selected for control must be competitive when introduced into the native environment. Therefore, several strains will have to be

Table 2 History of the Reduced Fertility achieved by Crosses between Male House Flies or Males plus Females bearing Heterozygous Translocations and Wild Type Flies (All Cages contained a Minimum of 200 Flies)

Cross	Fertility coefficient (%)	Accumulated fertility coefficient (%)
Control—wild type × wild type (for three generations)	100.0	100.0
9 Trans A ♀♀ × 9 Trans A ♂♂ × 1 wild type ♀ × 1 wild type ♂	10.3	10.3
$F_1 \times F_1$	30.3	3.1
9 Trans A ♀ × 9 Trans A ♂ × 1 F_1 ♀ × F_1 ♂	29.2	3.0
$F_2 \times F_2$	36.1	1.1
$F_2 \times F_2$ (no further additions)	34.2	1.0
Based on the % hatch of 17,223 total eggs and the emergence of 3,902 total adult flies.		
Control—wild type × wild type (for four generations)	100.0	100.0
9 Trans B ♀♀ × 9 Trans B ♂♂ × 1 wild type ♀ × 1 wild type ♂	20.5	20.5
$F_1 \times F_1$	53.7	11.0
Added 9 Trans B ♀ × 9 Trans B ♂ × 1 F_1 ♀ × 1 F_1 ♂	29.8	6.1
$F_2 \times F_2$	67.8	7.5
$F_2 \times F_2$ (no further additions)	36.0	2.2
$F_3 \times F_3$	86.0	6.4
$F_3 \times F_3$	63.1	1.4
Based on the % hatch of 14,217 total eggs and the emergence of 1,659 total adult flies.		
Control—wild type × wild type (three generations)	100.0	100.0
9 Trans A ♂♂ × 1 wild type ♀ × 1 wild type ♂	17.9	17.9
9 Trans A ♀♀ × 9 Trans A ♂♂ × 1 wild type ♀ × 1 wild type ♂	21.6	21.6
Added 9 Trans A ♂♂ × 1 F_1 ♀ × 1 F_1 ♂	34.1	6.1
$F_1 \times F_1$	31.4	6.8
Added 9 Trans A ♀♀ × 9 Trans A ♂♂ × 1 F_1 ♀ × F_1 ♂	23.6	5.1
$F_2 \times F_2$ (no further additions)	56.3	3.4
$F_2 \times F_2$	37.9	2.6
$F_2 \times F_2$ (no further additions)	32.5	1.7
Based on the % hatch of 10,761 total eggs and the emergence of 1,102 total adult flies.		
Control—wild type × wild type (one generation)	100.0	100.0
9 Trans C ♂♂ × 1 wild type ♀♀ × 1 wild type ♂	45.8	45.8
Control wild type × wild type (four generations)	100.0	100.0
4 Trans C ♂♂ × 1 wild type ♀ × 1 wild type ♂	42.0	42.0
$F_1 \times F_1$	82.2	34.5
Added 4 Trans C ♂♂ × F_1 ♀ × F_1 ♂	83.2	34.9
$F_2 \times F_2$	None	34.5
$F_2 \times F_2$ (no further additions)	None	34.9
$F_3 \times F_3$	None	34.5
$F_3 \times F_3$	None	34.9
Based on the % hatch of 8,833 total eggs and the emergence of 3,259 total adult flies.		

prepared so that the most viable in a particular natural setting can be selected.

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The Rhesus Syntenic Group in Man

THE two principal approaches to mapping human autosomes—the study of pedigrees and of cell hybrids—may sometimes complement each other.

Pedigree studies by Lawler and her co-workers[1] established a close linkage (0.03 morgans) between *Rh*, the rhesus set of blood group loci, and one of the loci, El_1, that can lead to elliptocytosis of the red cell. There seems to be, in addition, at least one isophenic, or mimicking, locus[2] which is not closely linked to *Rh*. Weitkamp, Guttormsen and Greendyke[3,4] have demonstrated that *Rh* is linked to *6PGD*, the polymorphic locus for 6-phosphogluconate dehydrogenase. The maximum-probability estimate of the map distance (taking no account of the sex difference uncovered by these authors) is about 0.24 morgans (0.13–0.36). The study of man/hamster cell hybrids has recently added PGM_1, the locus for one species of phosphoglucomutase molecules, to this syntenic group[5,6]. A high correlation was found in loss or retention of the human PGM_1 and human *6PGD* isozymes as studied in clones derived at various stages during the progressive loss of whole chromosomes (preponderantly human) from the hybrid cells.

To determine the sequence of the PGM_1, *Rh*, *6PGD* loci, thus shown to be on the same chromosome, I have estimated the map distances on a large section of the data tested during 1965–68 in my laboratory (then in Glasgow).

A set of aggregate lods (standardized likelihoods in logarithmic form) is given in Table 1 for the $Rh : PGM_1$ interval together with another set for the $PGM_1 : 6PGD$ interval. The lods of Weitkamp *et al.*[4] are used unmodified for the *Rh* : *6PGD* interval and no account has been taken here of a sex difference in the recombination fractions. From inspection alone, it would seem that *Rh* lies between the other two loci, and a full analysis, using the Bayesian methods of Renwick and Bolling[7], confirms this. The posterior odds on this ordering as opposed to any alternative, are 5 : 1. (The relative position of El_1 is unresolved until more substantial data are available to indicate its distance from PGM_1 and *6PGD*.)

If this ordering with *Rh* near the centre of the group is correct, the $Rh : PGM_1$ interval is estimated as 0.27 M (95% probability limits are 0.16 and 0.43) and it is thus the longest map distance to be well estimated directly in man. As the data come from one laboratory, it is likely that direct estimations of longer intervals—up to 0.35 M or beyond—are within the limits of the method when data from several laboratories are combined. The simple addition of the lengths of the two component intervals gives a reasonable estimate of a still longer interval length—$PGM_1 : 6PGD$ (over 0.50 M), but this is indirect. Direct estimation of the corresponding recombination fraction may give some indication of the strengths of genetical interference in man but a good estimate would require an enormous body of high quality data.

Table 1 Lods for Various Values of Recombination Fractions

	Recombination fraction						
	0.5	0.45	0.4	0.3	0.2	0.1	0
$6PGD : Rh^4$	0	1.322	2.722	5.023	5.335	0.602	$-\infty$
$Rh : PGM_1$	0	0.704	1.409	2.947	2.290	-5.370	$-\infty$
$6PGD : PGM_1$	0	0.016	0.032	0.099	0.053	-0.367	$-\infty$

Lods are standard likelihoods in logarithmic form to base 10.

Pedigrees: CADDY, CAFFN, CALMS, CAOOD, CAPEA, CAPEB, CATTS, CAWWR, CDKGK, CD1LL, CD2BL, CLACL, CLAGE, EA1ME, EA1MR, EB1BR, EB1GS, EL1RS, JM1MY, JN1AN, MX1BK, MX1IE, NP1.W, NP1.X, NP1AB, NP1AC, NP1U1, NP1U2, NP1U3, PE1DY, PE1LK, PE1MD, PE1PD, PE1YY, SSEDL, SSEGE, SSEGR, SSEMD, SSESE, SY1MD, TY3VA, TY4BE, TY4PN, V21AN, WM1ME, WM1WE, 9J.GN, 9JATN, 9JCMY, 9JTF1, 9JTF2.

In summary, pedigree methods suggest that *Rh* and El_1 lie between PGM_1 and *6PGD*. The necessary analyses might have been long delayed but for the hybrid-cell demonstration of synteny of PGM_1 and *6PGD*. *PeC*, the locus for peptidase C, has recently been added to this syntenic group[8].

A different hybrid clone, one between human and mouse cells, was used by Conover and Hirschhorn[9] to assign tentatively this syntenic group or, more exactly, one of its members—the PGM_1 locus—to a *C* group chromosome. Fluorescence techniques from Caspersson's laboratory and other new staining procedures should allow this *C* group chromosome to be more precisely identified.

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Alpha Rhythms in the Hyperkinetic Child

HYPERKINESIS is a poorly understood but common disorder of childhood the main features of which are excessive motor activity, a short span of attention, low tolerance of frustration and hyperexcitability, often resulting in learning difficulties and a poor motor performance even where intelligence is normal. The neurophysiological substrate of this disorder remains undefined and emotional factors have often been invoked as its sole basis. Some children with this syndrome improve when given central nervous system stimulant drugs; We have attempted to distinguish those children who are likely to improve from those who may not.

The reaction times of human subjects are shorter when the signal to respond is given during spontaneous beta waves than when it is given during spontaneous alpha waves[1]. Beta waves seem to represent a process of cortical excitation, such that they appear when stimuli are perceived as novel and disappear with habituation[2-4]. Alpha rhythms are said to represent an inhibitory process involving discharge of subcortical influences back into the cortex, and effecting the termination of cortical excitation associated with automatization or habituation of learned behaviour[2].

Alpha rhythms were therefore studied in a group of hyperkinetic children as a possible measure of increased attention span. Twenty-eight children between the ages of 5 and 12, recognized by history and examination to have hyperkinesis and decreased attention span without psychomotor retardation, were chosen. Subjective scoring by parents and school teachers and objective measurements of activity level, impulsivity, performance and coordination were obtained for each child at the beginning of the study. Intravenous dextroamphetamine (10 mg m^{-2} body surface area), methylphenidate (20 mg m^{-2} body surface area), or saline in equivalent volume was injected in random order, using double blind methods, into these twenty-eight children during an electroencephalographic (EEG) examination. The EEG responses were collected on magnetic tape 15 min before and 15 min after the injection, for 3 min each. Five control subjects were injected with one of the stimulant drugs (four had dextroamphetamine and one had methylphenidate), and their EEG responses were similarly recorded on magnetic tape. Silver electrodes were applied using the International 10–20 System and the eyes of the subjects were kept open throughout the experiment[5]. The potentials between P_4 and O_2 were analysed. A PDP-12 computer was used for the data analysis. The computer sampled four 17 s segments each from pre-injection and post-injection periods and performed the Cooley-Tukey fast Fourier transformation. The statistical test used the mean power of these four segments for pre-injection and post-injection periods.

Each of these children was put on oral therapy with dextroamphetamine, methylphenidate, or a placebo in random order, using double blind methods. Repeat subjective scoring and objective measurements of activity level, impulsivity, performance, and coordination were obtained at the end of a 3-week period. At that time all the subjects of the study were put on oral therapy with one of the central nervous system stimulant drugs (dextroamphetamine or methylphenidate) and followed during the next 2 yr.

Table 1 shows the correlations between response to oral therapy with central nervous stimulant drugs and the response of EEG alpha rhythms to the intravenous injection of these drugs. The final results are expressed by a ratio r, where $r=$

$$\frac{\text{EEG power alpha range (8 to 12 Hz) in the post-injection period}}{\text{EEG power in alpha range (8 to 12 Hz) in the pre-injection period}}$$

The results generally show an increase in alpha activity in those who responded well to oral drug therapy but not in those who did not. The Mann-Whitney U test was used to examine the difference between these two groups, which differed significantly ($P<0.05$). The control subjects injected with one of the central nervous stimulant drugs showed a consistent increase in alpha activity.

A retrospective analysis of the clinical effects noted immediately after injection of one of the drugs showed that those children who had a poor response to the oral therapy on follow-up had all shown a remarkable amount of restlessness, talkativeness, and inability to sleep.

Table 1 Response of Hyperkinetic Children to Central Nervous System Stimulants

	Drug injection			Saline injection
	Hyperactive children			
	Good response to the treatment	Poor response to the treatment	Normal controls	Hyperactive children
r values of the subjects	28.85	1.54	6.16	2.33
	8.20	0.68	2.77	1.27
	6.60	0.43	1.86	0.98
	5.13	0.42	1.45	0.98
	3.66	0.40	1.36	0.81
	1.85	0.13		0.78
	1.61			0.55
	1.49			
	1.32			
	0.76			
	0.74			
	0.49			
	0.48			
	0.40			
	0.37			

The basic neurophysiological defect in hyperkinesis of childhood seems to be a disorder of inhibitory mechanisms in the central nervous system such that irrelevant stimuli are not filtered out and the child is at the mercy of all the stimuli in his environment. Central nervous stimulant drugs seem to be able to activate or strengthen these inhibitory mechanisms. If alpha rhythm in the EEG is an index of relaxed wakefulness, habituation to a class of stimuli, should result in augmentation of alpha. The increase in alpha rhythms seen in those who responded well to the drugs supports this hypothesis.

This work was done while I was a research fellow in neurology at the Harvard University Medical School in Boston.

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Loss of the Sensory Process of an Insect Receptor at Ecdysis

CAMPANIFORM sensilla on cockroach legs are mechanosensitive sense organs associated with the exoskeleton which are thought to help coordinate the animal's walking movements[1]. Although the fine structure of campaniform sensilla has been elucidated[2], little is known about the morphogenetic changes they undergo during moulting. I wish to report initial findings of an electron microscopic investigation of the development of cockroach campaniform sensilla.

Each campaniform sensillum functions through a single primary sense cell—a large bipolar neurone with a cell body, of epidermal origin, which is in a pocket of endocuticle. Its axon goes directly to the central nervous system, but the dendrite is associated with the cuticle and has a tip containing a basal body which gives rise to a highly modified cilium. The distal portion of this, the sensory process, inserts into a thin cap of cuticle which is the site of mechanical stimulation[2]. The sensory process is a membrane-limited bundle of 350–1,000 parallel microtubules, which play a role in mechano-electric transduction in campaniform sensilla[3,4]. The intimate physical association of the sensory process with the cuticular cap of the sensillum raises the question of the fate of the sensory process at ecdysis.

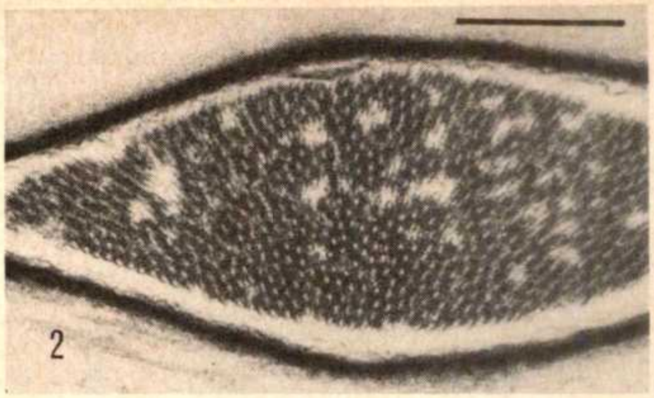

Fig. 2 Cross-section through the distal tip of a sensory process within an exuvium. Dense, amorphous material surrounds the microtubule walls (× 44,000). Scale = 0.5 μm.

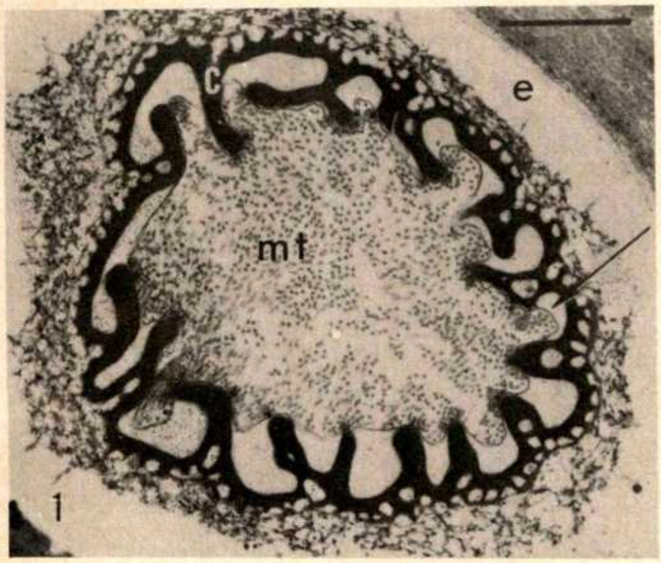

Fig. 1 Cross-section through a sensory process within an exuvium of the cockroach *Blaberus giganteus*. e, Extracellular space; c, cuticular sheath; mt, microtubules; arrow indicates cell membrane, which appears intact (× 17,000). Scale = 1 μm.

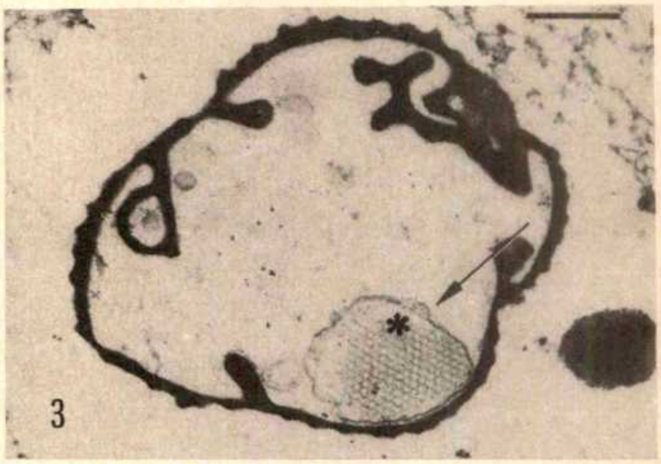

Fig. 3 Cross-section through a degenerating sensory process within an exuvium. Arrow indicates cell membrane. Microtubules have reorganized their structure into a crystalline body (asterisk) (× 25,000). Scale = 0.5 μm.

Fig. 1 provides clear evidence that the sensory process is shed at ecdysis, after which the cuticular sheath, plasma membrane, and 1,350 microtubules are present and appear intact (compare with Fig. 12, ref. 2). The microtubules, however, which are parallel *in vivo*, do not have uniformly cross-sectioned profiles in Fig. 1, suggesting that their proximal ends were floating free in the detached sensory process.

Fig. 2 is a cross-section through the tip of a moulted sensory process—the point at which it inserts into the cap of cuticle covering the sensillum which is displaced during mechanical stimulation. The electron-image of the moulted sensory process tip is indistinguishable from that of an intact campaniform sensillum (compare with Fig. 10 of ref. 2). The cell membrane, encompassed by an extracellular cuticular sheath, encloses a tightly packed bundle of more than 700 microtubules. The cross-sectioned microtubules are surrounded by dense, amorphous material which may participate in microtubule maintenance and initiation[2]. Although the cytoplasmic matrix seems to have left the sensory process (Fig. 1), the dense material remains at its tip, indicating a close association between the microtubules and the dense, amorphous material which surrounds their walls.

Fig. 3 shows a cross-section through a moulted sensory process which is apparently degenerating. The sensory process has greatly decreased in volume and occupies only a small portion of the space defined by the cuticular sheath. The microtubules have undergone rearrangement into a crystalline body which is reminiscent of crystals formed by the interaction of microtubule protein with vinblastine sulphate[5].

The loss of the sensory process of the campaniform sensillum at ecdysis is of considerable physiological significance especially when one considers that the microtubule-packed sensory process may be the transducer[3,4]. Before ecdysis, the cockroach has two cuticles. The old exocuticle, which will be shed, surrounds the new unsclerotized exocuticle, recently synthesized by underlying epidermal cells. At some time before the moult, the old sensory process must become nonfunctional, and the campaniform sensillum must establish a new functional connexion with the new cuticle.

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Thysanoessa inermis and *T. longicaudata* (Euphausiidae) as First Intermediate Hosts of *Anisakis* sp. (Nematoda: Ascaridata) in the Northern North Sea, to the North of Scotland and at Faroe

REPORTS[1,2] that live larvae of the nematode *Anisakis* from raw or inadequately cooked fish may cause eosinophilic granuloma of the alimentary tract in man have stimulated research into the ecology, taxonomy, physiology and pathogenesis of this genus in fish (natural second intermediate hosts), marine mammals (natural final hosts) and man and laboratory animals (abnormal hosts)[3,4]. But little attention has been paid to earlier stages in the life cycle or to a search for first intermediate hosts. A knowledge of early developmental stages of *Anisakis* might contribute to an understanding of geographical and other variations in abundance of the larvae in economically important fish. Uspenskaya[5] reported larval *Anisakis* in one of 855 specimens of the amphipod *Caprella septentrionalis* Krøyer, 1838, in one of 990 specimens of the decapod *Hyas araneus* (L.) and in one of an unspecified number of euphausiids *Thysanoessa raschii* (M. Sars, 1864) from the Barents Sea. Oshima *et al.*[6] found five larvae in 3,247 specimens of *T. raschii* and *T. longipes* Brandt, 1851, collected in the northern North Pacific Ocean and Bering Sea. Kagei[7], according to Gibson[4], mentioned *T. inermis* (Krøyer, 1846) as a first intermediate host of *Anisakis*.

Anisakis sp. larvae have been found in two species of *Thysanoessa* from the northern North Sea, north of Scotland and at Faroe. The euphausiids were extracted from routine plankton samples collected in 1969 and preserved in 4% formaldehyde on the fishery research vessels Scotia (now Scarba) and Explorer. A total of 2,730 specimens of *T. inermis* from twenty-seven localities are examined for larval nematodes. Eighteen of 1,335 specimens from twelve of these localities (Fig. 1) were infected with larval *Anisakis*, the incidence of infection at individual localities ranging from 0.5 to 4.0%. Examination of 950 specimens of *T. longicaudata* (Krøyer, 1846) from seven localities revealed infection in three of 335 specimens from two localities (Fig. 1), the incidence being 0.7 and 1.0%. This seems to be the first published report of larval *Anisakis* in *T. longicaudata* and also the first published record of them in any invertebrate in these waters.

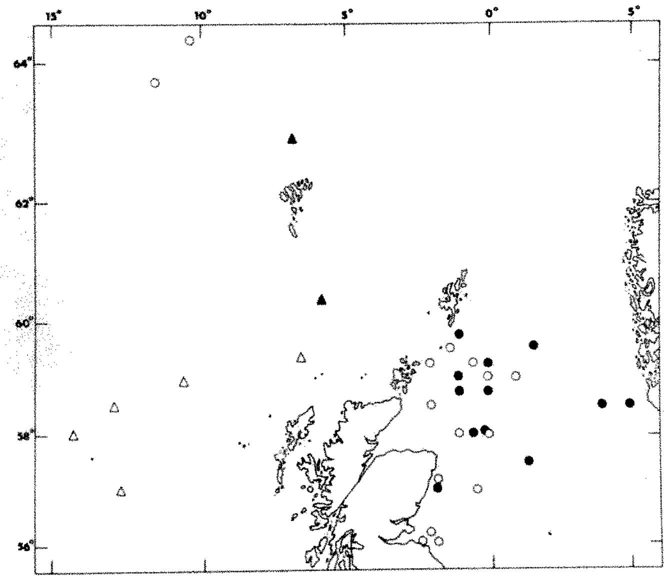

Fig. 1 Chart showing localities at which *Thysanoessa inermis* and *T. longicaudata* were collected and the distribution of infection with larval *Anisakis*. ●, Infected *Thysanoessa inermis*; ○, uninfected *T. intermis*; ▲, infected *T. longicaudata*; △, uninfected *T. longicaudata*.

Only one larva was found in each infected euphausiid; in preserved hosts the larva lay coiled in the haemocoel of the thorax, occasionally with the head or tail extending into the abdominal haemocoel. Observations on the behaviour of larval *Anisakis* in live euphausiids have not yet been possible. The larvae, probably second stage, were from about 5.1 to about 20.6 mm long and morphologically resembled third-stage larvae from fish, designated *Anisakis* sp. larva (1) by Berland[8]. Free-living second-stage larvae of *Anisakis* are comparatively small; such larvae experimentally hatched from eggs in sea water were ensheathed and about 0.22 to about 0.29 mm long (about 0.33 to about 0.37 mm long including the sheath). These probably exsheath after being eaten by euphausiids and grow to the lengths reported above; no euphausiid has so far been seen with larvae less than about 5 mm long. Larval *Anisakis* cannot be specifically identified as yet. There may be only the one species in the areas considered here, possibly *A. simplex* as defined by Davey[3].

Larval *Anisakis* were not seen in other euphausiids (463 specimens of *T. raschii*, 500 of *Nyctiphanes couchii* (Bell, 1853) and 488 of *Meganyctiphanes norvegica* (M. Sars, 1857)) collected at some of the localities where infected *T. inermis* or *T. longicaudata* were found. However, Dr P. van Banning (private communication) found an *Anisakis* larva, about 19.0 mm long, in one of 3,178 specimens of *M. norvegica* collected in 1970 from the northern North Sea.

Further work is necessary before any assessment can be made of the relative importance of *Thysanoessa* species, euphausiids in general and of other invertebrates in the life-cycle of *Anisakis*.

The only other larval nematodes seen during the present survey were *Contracaecum* sp.[8]; they occurred singly in some *T. raschii* and *N. couchii* (and in some chaetognaths *Sagitta elegans* Verrill, 1873) from the inshore locality off the north-east coast of Scotland where *T. inermis* infected with larval *Anisakis* were found (Fig. 1).

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Archaeopteryx Again

HEPTONSTALL[1] believes that my estimate of the mass of *Archaeopteryx*[2,3] (200 g) is far too light, and that a figure of 500 g is more likely.

He derives the figure of 500 g by comparing the linear dimensions of the bones of *Archaeopteryx* and *Columba livia*, and using the reconstruction by Heilmann[4] to suggest the body size. I should like to criticize this comparison for a number of reasons.

First, Heptonstall suggests that the average mass of *Columba livia* is 400 g, a value derived from Pennycuick[5], but this species seems to be rather variable in size, for Hartman[6] quotes the mean mass of six male specimens as 307 g and a female as 278 g, while Spector[7] gives the mean of four specimens as 270 g. There is therefore no particular justification in using a mean mass of 400 g for *Columba livia*, and it may well be that Pennycuick's animals were very large specimens. Equally, it is not known whether the skeletons of *Columba* which match in size that of *Archaeopteryx* come from large or small *Columba*.

Second, it is questionable whether *Columba* is a very good choice for comparison with *Archaeopteryx*. Pigeons have a higher proportion of their mass as flight muscle than other birds. On average, flight muscles contribute 17% of the mass in other birds, but about 25% of the mass in pigeons[6,8]. Further, the bones of *Archaeopteryx* and of jackdaws, *Corvus monedula*, can be matched for size as well as with *Columba livia*. The jackdaw is an insectivorous species, and is arboreal, so might be a reasonable comparison with *Archaeopteryx*. Greenewalt[8] suggests that this species weighs about 220 g, though to be fair one can be no more sure that this was the weight of the particular specimens whose skeletons are available than one could in the case of the pigeons.

A third point of disagreement concerns the reconstruction of *Archaeopteryx* by Heilmann[4]. Heptonstall has sent me the measurements he used and comparing these with a cast of the Berlin specimen of *Archaeopteryx* suggests that the body form shown in the reconstruction is much too deep dorso-ventrally, by perhaps 30%, and is also too long by 20%. I therefore remain convinced that a mass of about 200 g is a reasonable guess for *Archaeopteryx*[3].

Furthermore, Heptonstall's[1] reply to the comments by Bramwell[9] on the use of the formula

$$v = \sqrt{\frac{2L}{C_L \rho A}}$$

is seriously misleading. He says that if C_L and A are fixed, and L is set at its maximum value, then v is given its maximal value. This would be true of a fixed wing aircraft, but birds are not in this category. Pennycuick[10] has calculated for gliding pigeons a range of C_L from around 0.3 at high speeds to 1.3 at low speeds (and, indeed, as high as 2.8 when the pigeon is hovering); these changes in C_L are brought about by extending or partially folding the wings, thus altering A. Very similar results have been obtained with falcons[11]. (These values of C_L obtained by Pennycuick were calculated with the areas of the body strip and tail included in the figure for the wing area[1].) The velocity which Heptonstall originally calculated[12] is, then, the maximum diving speed with the wings fully extended, a rather improbable configuration. Out of interest, I recalculated the flying speeds using the same formula. For the "minimum" flying speed, $V_{\min}$, in level flight, I assumed that the wing was fully extended, and used a figure of 1.3 for C_L (based on Pennycuick's data[10]), while for the "maximum" flying speed $V_{\max}$, I assumed the lower figure of 0.3 for C_L and a wing area reduced by 30%, both of these figures also based on the performances of Pennycuick's pigeons[10]. The estimate of the mass of 200 g was used; the "wing area" included the body strip and the tail. These suggest a speed of 6.3 m/s for $V_{\min}$ and 15.3 m/s for $V_{\max}$. However, it must be emphasized that, quite apart from their highly speculative nature, these are not likely to have been the real minimum or maximum flying speeds. Stalling speed is likely to have been rather lower than the estimated $V_{\min}$, while a few wing beats might have slowed the bird even further, if it was trying to land rather than keep flying. Equally, a diving *Archaeopteryx* might well have achieved higher speeds than the estimated $V_{\max}$, if it had folded its wings more than I have suggested.

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DR HEPTONSTALL writes: I agree with Yalden that before comparing specimens of a living species with *Archaeopteryx* with a view to estimating the live weight of the latter, one must know both the weight and the skeletal dimensions of the living specimens. This relationship in Pennycuik's specimens of *Columba livia* is available from his paper[5] as he supplies the dimensions of the wing bones. As a result of recent correspondence on this subject[2,9] I have made a biometrical analysis of a specimen of the crow *Corvus corone corone* which weighed 553 g. Swinton[13] states that *Archaeopteryx* was similar in size to the larger common species, namely the raven, but this does not seem to be correct. In general my measurements indicate that the carrion crow was a little larger than *Archaeopteryx* and suggest a weight of 450–500 g for the latter.

My use[12] of the equation relating velocity to lift and wing area appears to require further clarification. I used this equation to determine the minimum radii of horizontal and vertical flight paths, these being determined by the maximum lift which the wings were permitted to generate. If we consider a horizontal circular path radius r with angle of bank θ, it follows from resolving the forces that

$$L \cos \theta = mg \qquad \text{(i)}$$

$$\text{and } L \sin \theta = \frac{mv^2}{r} \qquad \text{(ii)}$$

On fixing L at $2\,mg$ the banking angle is found from (i) to be 60°. Combining (ii) with the equation quoted by Yalden and eliminating v gives

$$r = \frac{2\,m}{2\,C_L\,\rho\,A \sin \theta}$$

As θ is fixed at 60° and m and ρ are constants, r is inversely proportional to the lift coefficient times the wing area. It follows therefore that for paths of minimum radius both C_L and A must have maximum values. My use of the term "maximum velocity"[1,12] was intended to apply only to these conditions. It is, of course, obvious that a higher velocity could have been reached on flight paths of greater radii if the wings were reduced in area and/or the lift coefficient was lowered. On this point I should like to correct a statement made by Yalden in which he says that "changes in C_L are brought about by extending or partially folding the wings, thus altering A". The lift coefficient is not determined by wing area but depends on the geometry of the wing and to some extent on the Reynolds number. The most convenient method of changing C_L is to vary the inclination of the wing relative to the airflow.

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Alteration of Sites on the Mammalian Sperm Surface following Capacitation

THE ovum cannot be penetrated by a spermatozoon until the latter undergoes a change termed capacitation[1] which, in the golden hamster, can be produced *in vitro* by incubation in various body fluids[2–4] including serum[5] and β-glucuronidase[6].

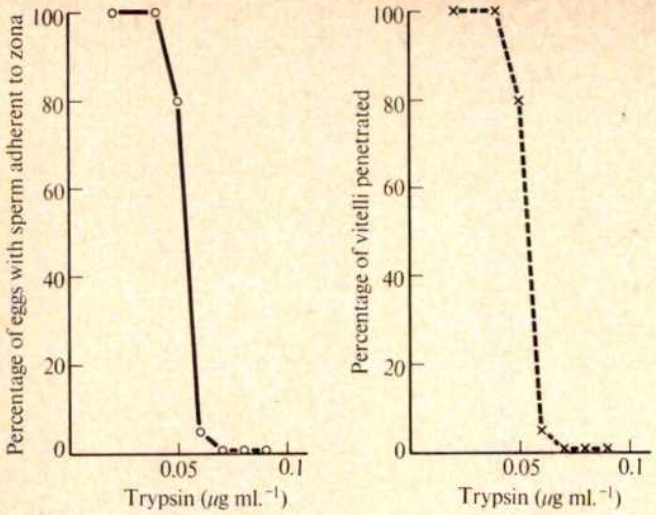

Fig. 1 Washed eggs were placed in 20 μl. drops of phosphate buffered saline with or without enzyme under oil at 37° C on a rocker in the CO_2 incubator for 1 h. Eggs were washed in 199 M before adding 20 μl. drops of capacitated sperm at a concentration of $1–3 \times 10^7$ motile sperm ml.$^{-1}$. After 90 min eggs were washed and scored as stated in the text. Twenty eggs were scored for each trypsin concentration.

The process involves vesiculation of the plasma membrane with the outer acrosomal membrane[7], which in turn seems to release egg-penetrating enzymes and exposes a surface which can fuse with the vitelline membrane of the egg[8]. As part of a series of investigations on the nature of these surface changes we have studied the effect of proteolytic enzymes on the adherence of sperm to eggs *in vitro*. Our results show that adherence of sperm to the zona pellucida is species specific both before and after capacitation. Capacitation alters the sperm surface, however, so that it will no longer adhere to trypsin-treated eggs.

Epididymal sperm from the golden hamster (*Mesocricetus auratus*) were collected in 199 M as already described[9] and capacitated by adding 20 μl. sperm suspension ($1–3 \times 10^7$ motile sperm ml.$^{-1}$), under mineral oil, to equal volumes of 199 M, containing the contents of an oviduct (17 h after treatment with human chorionic gonadotrophin (HCG), with eggs in cumulus). The culture was incubated at 37° C on a rocker (five to six oscillations min^{-1}) for 5 h. These conditions consistently yielded capacitated sperm. Ova which had been introduced by the oviduct contents were removed and other ova (20–22 h after HCG), free of cumulus, were then added to each drop. Cumulus was removed with hyaluronidase (450 USP units ml.$^{-1}$ of Dulbecco's phosphate buffered saline containing 1% polyvinylpyrrolidone). After the various incubation procedures, eggs were washed three times in 199 M, transferred to a slide, compressed slightly beneath a 'Vaseline-' edged cover glass and examined with a phase contrast microscope for adherence of sperm to the zona pellucida and penetration of sperm into the vitellus. To study sperm adherence to the isolated zona pellucida it was removed mechanically by a method described previously for mouse eggs[10].

The effect of trypsin (Crystalline, 196 U mg^{-1}, Worthington) and α-chymotrypsin (3 × crystalline, Nutritional Biochemicals Co.) on the interaction of capacitated sperm and whole eggs was determined as follows. Eggs were treated with enzyme, washed and exposed to capacitated sperm. As little as 0.05 μg trypsin ml.$^{-1}$ reduced sperm adherence and sperm penetration. The decline in adherence and penetration was sharp; both were eliminated at 0.06–0.09 μg trypsin ml.$^{-1}$ (Fig. 1). This experiment was conducted four times with similar results. That the block to adherence was due to enzymatic action was shown by the fact that pretreatment of eggs with 1 μg ml.$^{-1}$ trypsin plus 10 μg ml.$^{-1}$ soybean trypsin inhibitor for 2 h had no effect on adherence and penetration. α-Chymotrypsin also inhibited adherence and penetration, but at a higher concentration (0.2 μg–0.7 μg ml.$^{-1}$). Fig. 1 shows that the decline in penetration parallels the decline in adherence, suggesting that the former is due to the latter.

Table 1 Effect of Treating Isolated Zonae Pellucidae with Trypsin and Chymotrypsin on Subsequent Adherence of Capacitated Sperm

Treatment		Proportion of zonae with adhering sperm	
		Experiment 1	Experiment 2
None		20/20 (100%)	13/13 (100%)
Trypsin	0.10 μg ml.$^{-1}$	3/15 (20%)	—
	0.20 μg ml.$^{-1}$	0/15 (0%)	0/16 (0%)
	0.50 μg ml.$^{-1}$	0/20 (0%)	0/20 (0%)
α-Chymotrypsin	0.7 μg ml.$^{-1}$	3/11 (27%)	0/10 (0%)
	1.0 μg ml.$^{-1}$	0/7 (0%)	—

Eggs were exposed to phosphate buffered saline with or without enzyme for 60 min before sperm exposure.

To determine whether the entire egg or only the zona pellucida was involved, isolated zonae pellucidae were placed in phosphate buffered saline containing either trypsin or α-chymotrypsin. After 2 h the zonae were washed and exposed to sperm. The results (Table 1 and Fig. 2) show that capacitated sperm adhered to untreated zonae pellucidae but not to

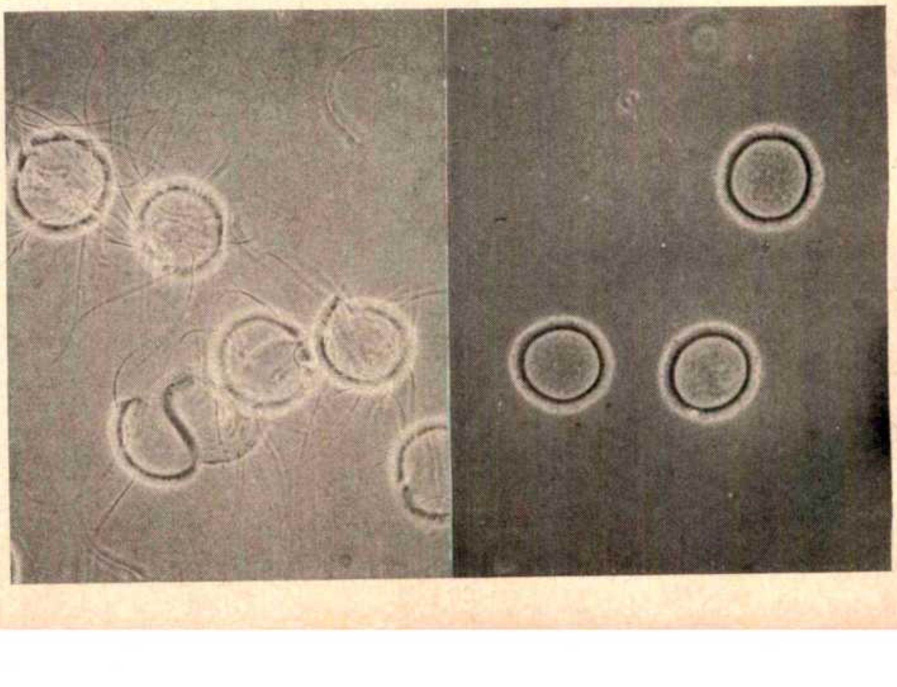

Fig. 2 Effect of exposing isolated zonae pellucidae to trypsin (1 mg ml.$^{-1}$) for 60 min on subsequent adherence of capacitated sperm. Left: control; right: trypsin-treated. (Phase contrast, × 120.)

those treated with trypsin. Thus it is clear that trypsin and α-chymotrypsin acted directly on the zona pellucida and that the effect was not mediated by the vitellus. This rules out any possibility that the block is produced by the release of cortical granules such as occurs in the zona reaction[11]. In another experiment the isolated vitelli (eggs without zonae pellucidae) were treated with trypsin and chymotrypsin for 1 hour and then exposed to sperm. Neither enzyme prevented capacitated sperm from entering the vitellus. These experiments show that there are sites for capacitated sperm-adherence on the zona pellucida which are extremely sensitive to trypsin and α-chymotrypsin and that sites on the vitellus are insensitive to these enzymes. The adherence of uncapacitated sperm, however, was unaffected by exposure of eggs to as much as 5 µg trypsin ml.$^{-1}$, a concentration about one hundred times greater than that which blocked the adherence of capacitated sperm. Because capacitated sperm preparations contained oviduct contents and uncapacitated sperm preparations did not, we examined the adherence between eggs and capacitated sperm which had been washed free of these materials by centrifugation. Such sperm behaved as if oviduct contents were present: they adhered to untreated ova but not to those previously treated with trypsin.

Many spermatozoa which had not previously been exposed to oviduct contents (zero time) adhered to the ova (Fig. 3). When sperm were exposed to oviduct contents for 60 min there was no adherence (Fig. 4). This was also true of sperm which were exposed to oviduct contents for similar periods and washed by centrifugation before they were combined with eggs. The sperm did not begin to adhere again until they had been in oviduct contents for 3 h (Fig. 4). Sperm left on eggs for 90 min also began to penetrate at 3 hours. Thus restoration of the ability to adhere appears to be linked with the sperm's ability to penetrate. By 5 h and frequently as early as 4 h, capacitation was completed as judged by penetration of virtually all eggs.

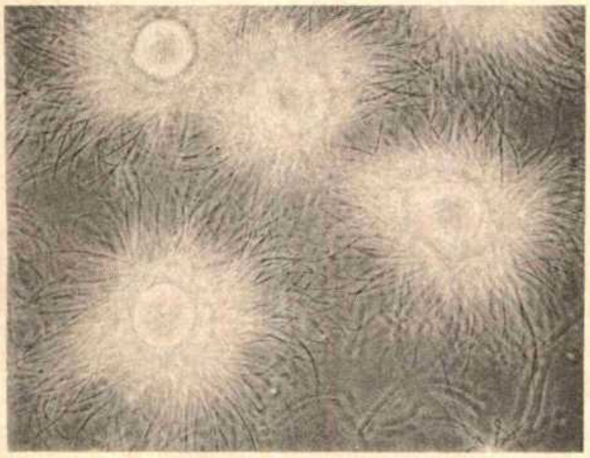

Fig. 3 Uncapacitated hamster sperm adhering to hamster ova. (Phase contrast, ×120.)

It is generally assumed that the sperm of one mammalian species will not fertilize the eggs of another, but little or nothing is known of the role of adherence in this specificity. We found that uncapacitated rat and mouse sperm failed to adhere to the zona pellucida of hamster ova. Capacitated mouse sperm, or capacitated hamster sperm, failed to adhere to the zona pellucida of hamster and mouse eggs, respectively. Species specific receptor sites must therefore be required for adherence of the sperm to the egg either before or after capacitation.

In our research on the nature of sperm adherence to the mammalian egg we are examining sperm glycoproteins, which belong to a class of substances known to be involved in a variety of "recognition" systems, for example, in the "homing" of lymphocytes[12]; as components of viral[13] and phytohaemagglutinin[14] receptors and in determining antigenic specificity[15]. Unlike the adherence of capacitated sperm to the zona pellucida, adherence to the isolated vitellus was unaffected by trypsin. This observation demonstrates clearly that the sperm use yet other adherence sites, or a modification of the same sites, to establish contact with the vitellus. Whether species specificity is involved has not yet been determined.

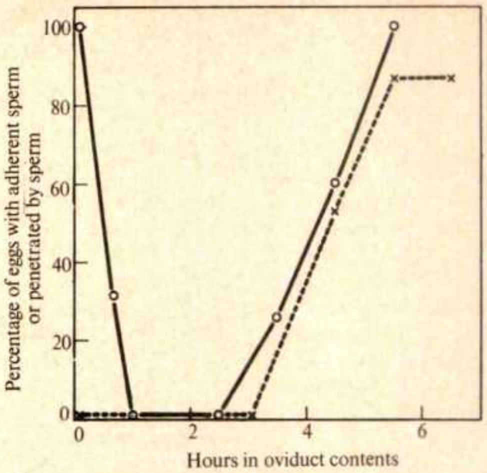

Fig. 4 Sperm were exposed to oviduct contents as described in text and ova were added at intervals. The adherence of sperm to these ova (○) and their penetration by sperm (×) were scored 30 and 90 min later, respectively.

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Urination as a Social Response in Mice

SOCIAL identification in mice appears to be based largely on the odour complex presented by an animal. The exact nature, as well as the relative importance and signal function of its components—metabolic, glandular and environmental—are still being investigated[1], but their efficacy as olfactory cues is reduced by applying scent to an animal[2] or by dabbing a mouse with the urine of another, which tends to elicit from conspecifics social responses in accordance with the "urine label"[3–5], at least as far as fighting or exemption from it is concerned. This suggests that the odour of urine present in some quantity overrides other olfactory cues, and that there may be a relationship between social behaviour and the extent of concurrent elimination. Although the active use of urination in territorial marking has long been known[6] and its occurrence in "open field" tests, where it is generally regarded as a fear response or an index of "emotionality", has received much experimental study, less is known about its incidence and import in social contexts, and the experiments reported here—carried out as part of a study of social sniffing—are an attempt to examine this point.

Eight male and eight female albino mice (TO strain), aged 6 months, and the same number of C57Bl mice, aged 10 months, were used. All were housed singly in 'Perspex' cages (30 × 12 × 12 cm) with absorbent flooring, which was periodically overlaid with a sheet of blotting paper fitting the cage floor. This was usually shredded up into nesting material, and no urination onto it was observed before the experiments during 3 min following its insertion. Social experience was provided two weeks before the first experiment by placing all mice of each strain into a 'Perspex' container (42.5 × 23 × 30 cm) with blotting paper flooring for two 30-min periods, because preliminary studies had suggested the existence of sex-typic sniffing and urinary responses, and these might be more evident in animals having some contact experience with conspecifics of both sexes. In order to make such experience comparable for all animals, any incipient fighting or mounting during these "socials" was immediately checked by gently separating the animals concerned. In four experiments carried out at intervals of 1–2 weeks, each animal's eliminative behaviour during a 3-min encounter with one male and one female partner was then recorded under four conditions: (1) as cage-owner presented with a male "visitor" (O + M); (2) as cage-owner presented with a female "visitor" (O + F); (3) as "visitor" placed in the home cage of a male (V + M); (4) as "visitor" placed in the home cage of a female (V + F). A balanced design was used throughout, equal numbers of animals starting in each condition, with location alternating and pair type arranged in ABBA sequence over 4 successive days. Urination bouts perceived as discrete events were recorded on a multi-channel event recorder and noted separately by a second observer. The quantity of urine passed was assessed by using, in each test, a fresh sheet of blotting paper secured to the cage floor by a narrow 'Perspex' frame, and subsequently measuring the area wetted by superimposing a cm^2 grid. The home cages used for testing were fitted with a temporary cover with a central opening through which "visitors" were lowered by hand. No urination was observed during such handling. In experiments 1 and 2, social interactions (sniffing, grooming, fighting and mounting) were simultaneously recorded; the results of these observations will be reported separately. In experiments 3 and 4 (with different pairs) a 3/8 inch wiremesh partition was inserted to keep the partners separated (the C57Bl mice could not be tested against each other in any other way, because fur clipping rather than dye-marking had to be used for their individual identification and this did not make them sufficiently discriminable in free interaction). Partition and hands were carefully washed between trials. Results in respect of urination during the tests are shown in Table 1.

Urination in these encounters is unlikely to have been a fear response, for it was generally most copious in male–female pairs where no fighting occurred, scanty in female–female pairs, and, among males, more abundant in cage-owners than in "visitors", though males were more often attacked in the latter role. Males urinated appreciably more in the presence of a female than in the presence of a male, even though the joint urine product of male–female pairs may be less than that of male–male pairs (experiment 4, Table 1*b*) because of the very small contribution of the female to the joint total; in the screen experiments (3 and 4) this was only 13% of the total for the pair. Females likewise tended to urinate more in the presence of a partner of the opposite sex, though at a much lower level. Placing a partition between the animals made no difference to this pattern. Though the C57Bl mice were much less responsive, in terms of urination as well as of social interaction, probably because of their age, they showed a similar trend.

The results, confirmed in current replications, suggest that urination, notably in male mice, may occur as a social response, involving sexual identification of the partner, which does not require close body contact. Urination may thus play an adaptive part in social encounters, being relatively ample in the presence of a partner of the opposite sex where continued proximity is of biological advantage; variable among males where drawing olfactory attention to himself would be unfavourable to a newcomer but advantageous to an animal on its home ground; and least among females where neither proximity nor spacing is required. It might thereby exert an effect on population density, group structure and individual interactions similar to

Table 1 Urination as a Social Response

(*a*) Mean urination bouts of male and female mice during 3-min encounter with another male (M) or female (F) in home cage (O) or partner's cage (V)

Experiment	Strains of S and partner	Males				Females			
		O+M	V+M	O+F	V+F	O+M	V+M	O+F	V+F
1	TO/TO	1.00	0.87	2.01	2.18*	1.00	1.31	0.62	0.56
2	TO/C57Bl	1.25	2.87	5.87	6.50†	1.87	0.82	0.37	0.50
	C57Bl/TO	0.37	0.37	2.00	1.87	1.37	1.25	0.37	0.00
3	TO/TO (screen)	3.00	2.00	6.00	8.00†	0.50	1.62	0.25	0.37
4	C57Bl/C57Bl (screen)	2.00	0.75	2.00	4.12	0.37	0.00	0.00	0.00

* $P<0.01$. † $P<0.005$. Friedman two-way analysis of variance.

(*b*) Amount of urine passed by same-sexed and opposite-sexed pairs during 3-min encounters (mean cm^2 of floor area wetted)

Experiment	Male/male pairs	Male/female pairs	Female/female pairs
1	9.81	17.40	5.44§
2	8.87	13.15	3.00‡
3	15.37	19.88	0.50§
4	5.75	4.50	0.00‡

‡ $P<0.025$. § $P<0.005$. Kruskal-Wallis one-way analysis of variance.

(*c*) Amount of urine passed by individual male and female mice confronting same-sexed and opposite-sexed partner (experiments 3 and 4; mean cm^2 area wetted)

	When cage-owner	When "visitor"
Male confronting male	8.12‖	2.43‖¶
Male confronting female	10.17	11.06¶
Female confronting male	0.90	2.25
Female confronting female	0.12	0.12

‖ $P<0.01$ (two-tailed). ¶ $P<0.005$ (one-tailed). Wilcoxon matched-pairs signed-ranks test.

that ascribed to agonistic behaviour[7], but with an additional positive role among opposite-sexed individuals which might correspond to attraction mechanisms of hormonal origin noted in primates[8,9], as well as those based on specialized scent glands[10], and could therefore serve as the starting point for the well-known "primer" effects of male odour upon female endocrine function[11–13].

The origin of such differential urination patterns could lie in mother–pup interactions, for females promote urination in pups by licking[14], and opposite-sexed offspring might learn to make different urinary responses to adult female odour. Relationships of an analogous kind have, indeed, been postulated for human psycho-sexual responses[15]. Among the more immediate causal factors may be perineal sniffing, which was significantly more prolonged, and preceded urination more often, in opposite-sexed pairs than in same-sexed pairs. The deployment of this eliminative behaviour is likely to vary according to age, social experience and probably other factors, and some of these aspects are now being investigated.

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Hierarchy of Water and Energy Turnover of Desert Mammals

MAMMALS inhabiting desert regions might be expected to have similar physiology, particularly in rates of water use. Groups of ungulates in the field, however, show a wide range of water consumption. We measured, over periods of weeks, the uninhibited intake of water and food by groups of animals grazing together on the same territory and this was integrated with metabolic water from oxidation of hydrogen. Using this approach[1] we found that buffalo (*Bos bubalus bubalis*) have the highest water turnover of any unstressed animal so far measured —200 ml./kg/24 h. *Bos taurus* in the same tropical climate were next in rank order, then *Bibos banteng* and the least water-demanding of the cattle group were *Bos indicus* (123 ml./kg/24 h). In the summer deserts of Australia and northern Kenya, the highest water turnover rates occurred in cattle, with sheep at about half their rate, goats somewhat less and camels (*Camelus dromedarius*) least in their water requirements, at half to one-third the rate of cattle[2]. In temperate environments the same rank order of genera and species was sustained. Because of different degrees of fatness (body solids, Table 1) it is useful to rank the animals by mol/l.$^{0.82}$, which relates to the number of molecules passing through the size-adjusted volumes of body water.

Antelope grazing with cattle on the Athi River plains of Kenya also showed a hierarchy of water turnovers (Table 1). Eland (*Taurotragus oryx*) and boran (*B. indicus*) cattle were equal in water demands, while kongoni (*Alcelaphus buselaphus*) and wildebeest (*Connochaetes gnou*) are comparable with sheep, at half the rate of eland, and an oryx (*Oryx gazella*) used water at a lower rate than camels.

Table 1 Content and Turnover of Water in Ruminants from Arid Arctic to Arid Tropics

		Body solids % body weight	Water turnover		
			ml./kg/ 24 h	mol/kg/ 24 h	mol/ l.$^{0.82}$/24 h
Arid subtropics (summer)					
Bos taurus	(6)	20.7 ± 4.83	161 ± 9.1	8.90 ± 0.5	29.1
Sheep (Ogaden fat-tail)	(7)	43.2 ± 3.36	102 ± 11.6	5.06 ± 0.64	18.7
Camel	(3)	28.5 ± 4.47	82 ± 4.9	4.56 ± 0.26	18.2
Equatorial arid (July)					
Bos indicus	(5)	28.0 ± 2.14	75 ± 4.9	4.16 ± 0.26	16.2
Eland	(5)	20.6 ± 2.15	79 ± 14.8	4.40 ± 0.82	14.4
Wildebeest	(1)	27.1	54	3.00	9.6
Kongoni	(2)	18.3	52	2.90	7.05
Arctic (April)					
Reindeer	(6)	23.6 ± 5.25	128 ± 29.7	7.1 ± 1.6	20.2
Moose	(1)	23.0	111	6.20	19.6
Sheep (Corriedale)	(5)	37.9 ± 5.57	62 ± 16.1	3.46 ± 0.9	11.2
Goats	(3)	33.0 ± 4.46	52 ± 5.4	2.90 ± 0.3	8.7
Musk oxen	(2)	33.5	35	1.90	7.9

Each group of animals was exposed to the same food supply and environmental conditions, but these differed between groups. The fatness of the animals is greater the more body solids present. Means ± s.d.

The cold desert of Alaska, with precipitation only 50–250 mm/yr, was also investigated. There, reindeer (*Rangifer tarandus*) had rates of water turnover as high as cattle, the moose (*Alces alces*) was somewhat lower but twice the rate of sheep and goats, while musk oxen (*Ovibos moschatus*) turned over water as slowly as camels (Table 1). Each region therefore showed a hierarchy of functional types so that animals differing three-fold in water demands inhabited the same dry areas. Survival times without water during summer in hot desert conditions are inversely proportional to water turnover: 3–5 days for cattle, for sheep 6–10 days and among camels 15–20 days[3].

A similar relationship of water turnover to survival time was found for desert dasyurid marsupials (Table 2). *Sminthopsis crassicaudata* turns over water at about three times the rate of *Dasycercus cristicauda* or *Dasyuroides byrnei*, but *Sminthopsis* dies in 3–4 days without water, while *Dasycercus* and *Dasyuroides* without water live indefinitely on insects or fresh meat. *Dasycercus* is centred on the arid inland but its range overlaps that of *Sminthopsis* which is most commonly found near wetter coastal areas. Rain forest dasyurids like *Antechinus* have high water turnover rates above 14 mol/kg$^{0.82}$/24 h. While resting at 25° C these species turn over about 5 mol of water for 1 mol of oxygen, but *Sminthopsis* uses over twice the water and oxygen turned over daily by *Dasycercus* per metabolic kilogram (kg$^{0.82}$ for water and kg$^{0.75}$ for oxygen). The desert rodents, *Pseudomys australis*, *Notomys cervinus* and *N. alexis*, use 3 mol water to 1 mol oxygen at 25° C but the rate of consumption of both these metabolites is between that of *Sminthopsis* and *Dasycercus*. These findings suggested a linkage between energy use and water turnover. It seemed also that animals evolved functionally for one environment might live successfully when displaced to the desert, although survival under deprivation would be short compared with types naturally selected in the desert. Functional organization like that of the camel presumably persists for millions of years in spite of environmental changes.

The metabolic rate or oxygen turnover of bovids when related[5] to kg$^{0.75}$ follows the same rank order as water turnover. *B. taurus* has a high metabolism (90–110 kcalories/kg$^{0.75}$/24 h), then comes *B. indicus* (80–90 kcalories), sheep (60 kcalories), goats[5], with camels[6] (50 kcalories/kg$^{0.75}$/24 h) lowest in rate of energy use. Among antelopes, the eland (110 kcalories) has a high metabolic rate like cattle but kongoni are lower (80 kcalories) in the range of sheep. Reindeer (102 kcalories/kg$^{0.75}$/24 h) also have high rates of oxygen consumption like cattle[7], but the rate of musk oxen is not known. Thus the ranking for water and oxygen turnover follows the same hierarchy, in each group and environment, as among the dasyurids.

Table 2 Water Turnover and Oxygen Consumption of Dasyurid Marsupials and Australian Rodents

			Water turnover/24 h		Pulmocutaneous evaporation/24h	Oxygen consumption/24 h	
		Weight	ml./kg	mol/l.$^{0.82}$	ml./kg	l./kg	mol/kg$^{0.75}$
Dasyurids							
Sminthopsis crassicaudata	(8)	17.4 ± 2.3	460.8 ± 68.4	17.2 ± 1.9	234	112.9 ± 13.0	1.91 ± 0.24
Dasycercus cristicauda	(35)	86.9 ± 22.1	133.9 ± 36.0	6.7 ± 1.2	95	36.1 ± 6.0	0.87 ± 0.16
Dasyuroides byrnei	(5)	130.0 ± 18.0	124.9 ± 22.1	7.2 ± 1.1	58	29.8 ± 5.8	0.81 ± 0.19
Rodents							
Notomys alexis	(9)	34.9 ± 3.7	192.4 ± 56.0	9.3 ± 4.3	86	74.4 ± 21.3	1.26 ± 0.24
Notomys cervinus	(11)	41.2 ± 3.1	149.0 ± 55.4	7.4 ± 1.9	77	65.0 ± 5.1	1.30 ± 0.18
Pseudomys australis	(10)	49.9 ± 12.1	139.0 ± 25.9	6.3 ± 1.3	89	62.7 ± 13.9	1.32 ± 0.25

Means and s.d.

The measurements were taken at temperatures near 25° C, with the animals at rest. Oxygen consumptions were averages over 1 h, and the water over 3–7 days.

The published determinations of metabolic rate[8] in birds show that passerines have higher oxygen consumption rates than non-passerine birds, and that the water intake of passerines[9] is correspondingly greater for the same size of bird than in non-passerines. Similar relationships seem to hold among plants in wet or dry habitats.

Other rate functions apparently linked to this system are the passage of labelled water from the rumen to blood, pulmocutaneous evaporation and the response of kidneys to vasopressin. Tritiated water moves rapidly from rumen to plasma in cattle so that plasma levels may reach as high as 90% of the equilibration value by 1 h, but in sheep only 50–60% of the final value is achieved in 1 h and the process is very slow in the camel with 25% in 1 h. These rates are presumably functions of the permeability of the rumen, but they follow the same rank order as water and oxygen metabolism. Evaporative transpiration of water through the skin and lungs ranks with water and energy turnover rates in small desert marsupials and rodents (Table 2) which do not have sweat glands. Similarly a standard reduction of diuresis or the increased excretion of potassium by ruminants infused with vasopressin requires fifty times more vasopressin in cattle than in the camel, while sheep or kongoni require three times the dose of camels, so that renal sensitivity to vasopressin is inversely proportional to water turnover. All these functions may be linked in the hypothalamus, but they also require coordinated cellular rate constants for handling water and energy.

Such disparate metabolic and physiological organizations in arid zone animals may arise from Pleistocene redistribution of genera[10]. Cattle radiated from Indochina where they seem to have evolved as wet tropical animals from ancestors of the guar and banteng. *Bos indicus* is less water dependent than other cattle, but all bovids whether in wet, cool, hot or dry environments appear to retain high metabolic and water turnovers. Sheep and goats evolved in dry mountains[11] but retain a rate of turnover of water and energy in hot or cold deserts intermediate between camel and cattle. The camel evolved in a North American desert and, in spite of migration through northern Asia, it still retains its desert functions and rates of metabolism. Water and energy handling rates may persist for millenia after migration to a different environment. Such functional diversity needs to be taken into account in introducing animals to new areas, or in making models of functions for a particular niche.

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Birth Rank and Mental Illness

Barry and Barry[1] observed in a sample of American schizophrenics an over-representation of first borns in small sibships and later borns in large ones. On this evidence they hypothesized that the more severe pressure of parental expectation on first borns of small sibships and the relative parental rejection of later borns in large ones might contribute to the development of schizophrenia in adult life. Erlenmeyer-Kimling *et al.*[2] reported that the same trend was observed about as frequently in studies of non-schizophrenics, and Price and Hare[3] suggested reasons for such a trend being present in the British population as a whole and demonstrated it in a large sample of non-schizophrenic patients[4]. They noted that the extent of the deviation varied with year of birth. They later showed that the birth rank distribution of a large sample of British schizophrenics differed significantly from that of a sample of neurotics, having the same year of birth distribution and which they assumed to be representative of the general population[5]. In sibships of two to four there was a comparative excess of schizophrenics in the later birth ranks. Hinshelwood[6] attempted to explain this finding by postulating that, in schizophrenia, there is a specific over-representation of the penultimate birth rank. To account for the vulnerability of the penultimate sibling he revived Adler's "dethroned monarch" theory, suggesting that an unwanted last child may be an especial trauma to its predecessor. He summed data of six previous studies (four American, one Canadian and one British), and demonstrated in the total sample an over-representation of the last-but-one position. Hare and Price[7] considered this to be a chance effect of combining studies carried out at different times and in different countries. Hinshelwood should be further criticized for combining data on patients diagnosed as schizophrenic in America and Britian. A recent patient[8] was videotaped and diagnosed as schizophrenic by 69% of American psychiatrists but only 2% of British ones. The latest

Table 1 Percentage Birth Rank Distribution by Sibship Size by Year of Birth of the General Population Control Sample

Sibship size	Year of birth	Birth rank 1	2	3	4	5	6	7	8	9	10	Not known	Total
2	Before 1910	45.5	54.5									5	49
	1910–29	53.9	46.1									4	158
	1930–49	61.3	38.7									3	274
3	Before 1910	29.2	43.1	27.8								2	74
	1910–29	35.9	33.8	30.3								3	198
	1930–49	31.2	32.8	36.0								3	253
4	Before 1910	22.0	28.0	24.4	25.6							4	86
	1910–29	22.8	30.1	28.0	19.2							5	198
	1930–49	28.6	22.2	25.9	23.2							1	186
5	Before 1910	13.8	20.0	20.0	26.2	20.0						4	69
	1910–29	15.3	14.0	23.3	22.7	24.7						5	155
	1930–49	19.4	14.9	18.7	24.6	22.4						1	135
6	Before 1910	16.0	13.0	20.0	19.0	10.0	22.0					3	103
	1910–29	10.8	19.6	16.2	14.9	16.9	21.6					5	153
	1930–49	10.4	11.5	16.7	19.8	16.7	25.0					2	98
7	Before 1910	14.1	7.6	22.8	16.3	14.1	15.2	9.8				1	93
	1910–29	16.2	10.8	15.3	9.9	11.7	21.6	14.4				2	113
	1930–49	4.3	11.4	7.1	24.3	17.1	10.0	25.7				2	72
8	Before 1910	14.0	10.5	11.6	14.0	5.8	15.1	10.5	18.6			3	89
	1910–29	7.5	6.5	14.0	10.8	15.1	5.4	24.7	16.1			2	95
	1930–49	6.1	14.3	4.1	10.2	12.2	22.4	14.3	16.3			0	49
9	Before 1910	17.2	10.9	6.3	18.8	10.9	6.3	12.5	7.8	9.4		3	67
	1910–29	7.8	14.1	9.4	9.4	15.6	7.8	15.6	6.3	14.1		2	66
	1930–49	9.4	12.5	3.1	6.3	6.3	9.4	12.5	21.9	18.8		1	33
10	Before 1910	6.3	8.3	4.2	14.6	14.6	12.5	8.3	10.4	6.3	14.6	3	51
	1910–29	14.6	12.5	2.1	8.3	14.6	10.4	8.3	10.4	6.3	12.5	0	48
	1930–49	4.2	4.2	12.5	0.0	8.3	20.8	8.3	12.5	16.6	12.5	0	24

Table 2 Total Birth Rank and Reverse Birth Rank Distribution by Year of Birth for the General Population Control Sample

Birth rank	1	2	3	4	5	6	7	8	9	10	Not known	Total
Before 1910	123 18.8%	131 20.1%	110 16.8%	103 15.8%	55 8.4%	59 9.0%	30 4.6%	26 4.0%	9 1.4%	7 1.1%	28	681
Total 1910–29	273 23.6%	278 24.0%	209 18.1%	124 10.7%	106 9.2%	71 6.1%	53 4.6%	24 2.1%	12 1.0 %	6 0.5%	28	1,184
1930–49	343 30.9%	279 25.1%	190 17.1%	119 10.7%	68 6.1%	50 4.5%	31 2.8%	18 1.6%	10 0.9%	3 0.3%	13	1,124

$\chi^2 = 84.3847$, d.f. = 18. $P < 0.001$.

Reverse birth rank	Last	−1	−2	−3	−4	−5	−6	−7	−8	−9	Not known	Total
Before 1910	138 21.1%	129 19.8%	115 17.6%	79 12.1%	68 10.4%	52 8.0%	33 5.1%	21 3.2%	15 2.3%	3 0.5%	28	681
Total 1910–29	282 24.4%	316 27.3%	218 18.9%	123 10.6%	94 8.1%	54 4.7%	34 2.9%	17 1.5%	11 1.0%	7 0.6%	28	1,184
1930–49	327 29.4%	370 33.3%	193 17.4%	117 10.5%	54 4.9%	24 2.2%	11 1.0%	10 1.0%	4 0.4%	1 0.1%	13	1,124

$\chi^2 = 150.0827$, d.f. = 18. $P < 0.001$.

Table 3 Percentage Birth Rank Distribution by Sibship Size for the Total Patient and Control Samples

Sibship size		Birth rank											
		1	2	3	4	5	6	7	8	9	10	Not known	Total
2	Patients	55.4	44.6									0	872
	Controls	57.2	42.8									12	482
3	Patients	34.9	33.0	32.1								11	1,020
	Controls	32.9	34.5	32.6								8	527
4	Patients	25.3	26.8	23.3	24.6							9	913
	Controls	25.0	26.5	26.5	22.0							10	470
5	Patients	17.2	19.4	19.7	22.0	21.8						7	816
	Controls	16.6	15.4	20.9	24.0	23.1						10	360
6	Patients	16.0	15.7	15.5	17.1	16.4	19.3					8	691
	Controls	12.2	15.4	17.4	17.4	14.8	22.7					11	355
7	Patients	9.7	11.0	14.4	15.0	12.2	17.3	20.3				4	530
	Controls	12.4	9.9	15.7	16.1	13.9	16.4	15.7				5	279
8	Patients	8.5	9.8	9.8	9.8	13.7	11.4	17.8	19.8			8	395
	Controls	10.0	10.0	10.9	11.7	10.9	12.6	17.0	17.0			5	235
9	Patients	6.7	10.9	8.6	13.9	10.5	10.5	9.7	13.5	15.7		4	271
	Controls	11.7	12.3	6.8	12.3	11.7	7.4	13.6	11.1	13.0		6	168
10	Patients	5.1	8.3	6.9	11.5	9.7	10.1	11.1	7.4	17.1	12.9	2	219
	Controls	9.1	9.1	5.0	9.1	13.2	13.2	8.3	10.7	8.3	14.0	3	124

Table 4 Total Birth Rank and Reverse Birth Rank Distribution for the Total Patient and Control Samples

Birth rank	1	2	3	4	5	6	7	8	9	10	Not known	Total
Patients	1,425 (25.1%)	1,371 (24.2%)	952 (16.8%)	696 (12.3%)	454 (8.0%)	317 (5.6%)	226 (4.0%)	126 (2.2%)	79 (1.4%)	28 (0.5%)	53	5,727
Controls	742 (25.3%)	690 (23.5%)	509 (17.4%)	347 (11.8%)	230 (7.8%)	180 (6.1%)	114 (3.9%)	70 (2.4%)	31 (1.1%)	17 (0.6%)	70	3,000

$\chi^2 = 4.3649$. d.f. $= 9$. N.S.

Reverse birth rank	Last	−1	−2	−3	−4	−5	−6	−7	−8	−9	Not known	Total
Patients	1,494 (26.3%)	1,550 (27.3%)	1,020 (18.0%)	676 (11.9%)	410 (7.2%)	263 (4.6%)	137 (2.4%)	77 (1.4%)	36 (0.6%)	11 (0.2%)	53	5,727
Controls	750 (25.6%)	817 (27.8%)	528 (18.0%)	320 (10.9%)	216 (7.3%)	130 (4.4%)	79 (2.7%)	49 (1.7%)	30 (1.0%)	11 (0.4%)	70	3,000

$\chi^2 = 10.7263$, d.f. $= 9$. N.S.

Table 5 Percentage Birth Rank Distribution by Sibship Size of the Psychotic Patients compared with a Year of Birth Based Expected Distribution derived from the Control Sample (Table 1)

Sibship size		Birth rank											
		1	2	3	4	5	6	7	8	9	10	Not known	Total
2	Observed	58.4	41.6									0	89
	Expected	56.7	43.3										
3	Observed	40.7	28.3	31.0								4	117
	Expected	33.3	34.7	32.0									
4	Observed	22.0	26.0	28.0	24.0							1	101
	Expected	24.6	27.2	26.7	21.5								
5	Observed	16.0	15.0	17.0	20.0	32.0						0	100
	Expected	16.1	15.3	21.5	23.8	23.3							
6	Observed	15.4	14.1	7.7	25.6	17.9	19.2					0	78
	Expected	11.8	16.0	17.2	17.1	15.3	22.6						
7	Observed	15.2	3.0	13.6	9.1	18.2	18.2	22.7				0	66
	Expected	13.0	10.1	15.4	14.8	13.5	17.3	15.8					
8	Observed	6.4	8.5	10.6	4.3	14.9	4.3	21.3	29.8			1	48
	Expected	9.0	9.2	11.3	11.5	12.0	11.6	18.7	16.8				
9	Observed	7.9	10.5	2.6	13.2	21.1	7.9	15.8	7.9	13.2		1	39
	Expected	10.6	12.9	7.2	11.1	12.3	7.8	14.1	10.3	14.0			
10	Observed	10.7	3.6	7.1	3.6	10.7	7.1	7.1	10.7	28.6	10.7	0	28
	Expected	10.3	10.1	3.8	10.4	14.1	12.0	8.3	10.5	7.0	13.4		

$\frac{(O-E)^2}{E}$ sibs of 2, 0.1057, d.f. $=2$, N.S.; sibs of 3, 3.2297, d.f. $=3$, N.S.; sibs of 4, 0.6817, d.f. $=4$, N.S.; sibs of 5, 4.8140, d.f. $=5$, N.S.; sibs of 6, 9.1392, d.f. $=6$, N.S.; sibs of 7, 8.1937, d.f. $=7$, N.S.; sibs of 8, 9.9374, d.f. $=8$, N.S.; sibs of 9, 4.3602, d.f. $=9$, N.S.; sibs of 10, unreliable.

Table 6 Total Birth Rank and Reverse Birth Rank Distribution of the Psychotic Patients compared with a Year of Birth Based Expected Distribution derived from the Control Sample (Table 1)

Birth rank	1	2	3	4	5	6	7	8	9	10	Not known	Total
Total observed	167 25.3%	132 20.0%	103 15.6%	78 11.8%	76 11.5%	34 5.2%	33 5.0%	20 3.0%	13 2.0%	3 0.5%	7	666
Total expected	157.7 23.9%	151.4 23.0%	117.0 17.8%	81.0 12.3%	58.5 8.9%	40.8 6.2%	26.9 4.1%	14.8 2.2%	7.3 1.1%	3.8 0.6%		

$\chi^2 = 19.0184$, d.f. $= 10$. $P < 0.05$

Reverse birth rank	Last	−1	−2	−3	−4	−5	−6	−7	−8	−9	Not known	Total
Total observed	180 27.3%	179 27.2%	132 28.0%	61 9.3%	48 7.3%	27 4.1%	16 2.4%	9 1.4%	4 0.6%	3 0.5%	7	666
Total expected	164.5 25.0%	178.0 27.0%	122.4 18.6%	73.9 11.2%	52.2 7.9%	29.4 4.5%	18.5 2.8%	10.2 1.5%	6.9 1.0%	2.9 0.4%		

$\chi^2 = 6.7060$, d.f. $= 10$. N.S.

study of Hare and Price[5] is far from conclusive for, as Barry and Barry[9] have correctly pointed out, a sample of neurotics, or of any other non-schizophrenic patients, may well differ from the general population by birth rank distribution.

It is now clear that the estimation of expected birth rank distributions by the Greenwood–Yule[10] procedure, which involves assuming an even distribution within each size of sibship, must be replaced by the direct comparison of psychiatric patients and an appropriate general population sample. The findings of such a comparative study from the north-east of Scotland are presented here. Tables 1 and 2 clearly show that, in the general population sample, there was a significant relationship between year of birth and both birth rank and reverse birth rank. Tables 3 and 4 present a detailed comparison of the birth rank distribution, for sibships of two to ten, of psychiatric patients and controls of similar year of birth distribution. In both samples there was an excess of first borns in sibships of two and of later born siblings in the larger sibships. The total birth rank and reverse birth rank distributions were strikingly similar in the two samples. The psychotic patients presented in Tables 5 and 6 were predominantly schizophrenic (ICD code numbers 300, 301.0, 301.2 and 303). They did not correspond by year of birth distribution with the control sample. Their birth rank distribution was therefore compared with a year of birth based expected distribution derived from the control sample. An excess of first borns in sibships of two and of later born siblings in the larger sibships was both observed and expected. The observed did not significantly exceed the expected in the later birth ranks of sibships of two to four. In the penultimate birth rank the observed and expected differed by only 0.2%.

It must be concluded that the positive findings of previous studies were due entirely to failure to take into account the very considerable effect of year of birth on birth order distribution and failure to compare patient samples with general population controls.

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A Non-parametric Alternative to d′

THE signal-detection theory propounded by Tanner and Swets[1] has proved immensely valuable and illuminating in a wide range of psychological contexts[2]. It first gained popularity because of two signal merits: it accounted for the previously unexplained forms of the receiver operating characteristic (ROC) curve, and it enabled a numerical measure (d′) to be put to the discriminability of stimuli.

The theory, however, makes a number of assumptions which are not necessary and may not always be true. Specifically, it is supposed that stimuli are represented internally by populations of signals which are both Gaussian in form and equal in variance. The general form of the ROC curve, however, is also predictable if other distributions are assumed—indeed, any which have a central "bulge" and longish tails. It is also not strictly necessary to assume equality of variance and there is some reason[3] to suppose that variances are not equal. Unfortunately, it has not so far proved possible to distinguish experimentally between models which make the strict assumptions and those which do not. Further, attempts to examine subjects' responses in detail[4] indicate that there may be considerable individual departures from the requirements of the model.

In practice, psychologists generally wish to ask two questions in a signal detection situation. These are: first, what is the relation between omissions and false positives—that is, what is the shape of the ROC curve? Second, how discriminable are the stimuli, or, more generally, how does the ease of distinguishing A from B compare with that of distinguishing A from C? The first question is generally, and satisfactorily, answered by asking for subjects' confidence ratings and so plotting the ROC curve directly. It is now usual to use d′ from the second question.

Unfortunately, the use of this measure may, as we have seen, imply many assumptions which are simply not known to be true. The assertion (say) that d′ for A and B is 1.61 and for A and C is 2.03 has a somewhat deceptive innocence. We are not merely asserting that it is easier to distinguish C than B from A. We are asserting that these quantities are represented to the subject internally by Gaussian distributions of percepts, whose variances are all equal and, moreover, whose form is perfectly known by the subject. This is rather more than is warranted by our current knowledge. There seems, then, to be a need for a measure of discriminability which does not imply commitment to a particular model. Such a non-parametric measure should have the properties of being quick and simple to use, and should be monotonically related to d′, so that the rank ordering of results may be unaffected whichever measure is used.

For recognition experiments, Brown[5] proposed just such an index. Pleasing though it was, however, it had originally the limitation that a number of examples of "noise" and of "signal and noise" had to be presented simultaneously. It is often desirable, and sometimes unavoidable, to present items sequentially. Brown has therefore modified his index (personal communication, 1971) for this condition. It is, however, computationally a trifle laborious, and there is clearly a need for a measure which is consistent and which can be derived as simply as possible from the data for the ROC curve. The following alternative is therefore suggested.

Let subjects be presented with a sequence of samples of As and Bs. They are asked to give confidence ratings from $1=$ certainly A to $r=$ certainly B. Compute the mean rating for As ($=N$, say) and for Bs ($=n$, say). For perfect discrimination, $N=1$, $n=r$; for random responses $N=n$, clearly. Let C be the index, defined as

$$C = \frac{n - N}{r - 1}$$

It can be shown that C is monotonically related to d′, and it is obvious that $C=1$ for perfect discriminability, 0 for random response, and lies between 0 and -1 for consistent error.

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Wishful Thinking of Turgor

Reviewing work by Rayle *et al.*[1] a correspondent has written[2] that plant cell growth is a simple process, and continues, "There is a strong osmotic tendency for water to enter a . . . growing cell, but this is prevented by the rigidity of the cellulose walls". (Hydroxyproline bridges in the wall limiting growth are located in the amorphous matrix; hence a unique role of cellulose as resistance in the wall is questionable[3].) The first sentence is dubious. Cleland[4], however, has expounded the matter: "This potential for extension can . . . be converted by turgor pressure into . . . wall extension". This adds to the doubts because the rigidity of the walls preventing the entry of water is the cause of the turgor pressure, which arises as a consequence of the resistance of the wall to an expansion. How then can the turgor pressure cause expansion? A simple answer is given by Green *et al.*[5]: "Plant cell growth is . . . believed to be the result of a driving force, turgor pressure, acting on a yielding cell wall". Many authors prior to them have written the same for 40 years, usually without the cautious "believed to be".

The conditions conducive to expansion are expressed in the following universally accepted way: $\psi_c = P - \pi \ldots$, in which ψ_c means the water potential of the cell, P, turgor pressure, π, osmotic potential, and other terms have been left out in this context[6].

If the tissue is in equilibrium with the ambient medium $\psi_m = \psi_c$, where ψ_m denotes the water potential of the medium. Actually the water permeability is usually so high that these two are always equal. That is why the first quoted phrase of *Nature's* correspondent is ambiguous. The origin of P is, as mentioned, the resistance of the cell wall to expansion. A cell ceases to take up water when $\psi_m = \psi_c$ and P reaches a maximum. Turgor is built up because there is an expansion. Thus turgor does not cause expansion and is not the driving force. What this is I shall show later.

First I shall consider growth. It begins with a loosening of the wall, demonstrated by Cleland and many others. It can certainly take place in different ways[7]. It implies that the resistance to an expansion decreases, P would attain a value P_x with $P > P_x$. Thus $\psi_m > \psi_{cx} = \mathrm{P}_x - \pi \ldots$. This causes an immediate expansion. The driving force is the difference $\psi_m - \psi_{cx}$. After expansion $\psi_m = \psi_c = P' - \pi' \ldots$, with P' and π' lower than P and π. This is elementary and was formulated in 1920 with other symbols. The driving force of any expansion is a difference in water potentials. Expansion is due to water uptake. Volume changes during growth should best be expressed in terms of water fluxes[8]. Unfortunately, the phrase "turgor expands the cell" was coined in 1931 and has been copied dogmatically in untold articles, although the mistake has been pointed out repeatedly[9,10].

What the erroneous opening "turgor expands the cell" may lead to is shown by Green *et al.*[5] who assume as an axiom or a corollary that growth (r) is proportional to P: $r = mP$. Since experiment fails to submit to the assumption, they introduce a correction factor, Y, called yielding threshold: $r = m(P - Y)$. This does not suffice because growth is practically independent of turgor. Thus they assume that Y shifts with P, otherwise $P - Y$ will not remain constant. It seems to me that little is left of the proportionality between P and growth in this instance.

The mistake made since 1931 is to regard the cell as something existing in an empty space, disregarding the ambient medium and external hydraulic pressures[5].

The literature on plant cell growth would certainly improve if the notion of turgor expanding the cell was abandoned and replaced by accepted equations for water balance or fluxes. They must be valid in growing as well as non-growing cells, perhaps with the addition of terms denoting cell wall changes[11] in growing cells.

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BOOK REVIEWS

Kammerer *Redivivus*

The Case of the Midwife Toad: The Paul Kammerer Controversy. By Arthur Koestler. Pp. 187+10 photographs. (Hutchinson: London, September 1971.) £2.

OF all the gadflies that have harassed the community of science in recent years, none has been more stimulating than Arthur Koestler. He has always been at his best when taking learned snipes at scientific orthodoxies. In *The Case of the Midwife Toad,* he follows true to form with a uniquely constructed attack on neo-Darwinism.

The vehicle for his argument is the tragic case of Dr Paul Kammerer (1880–1926). Kammerer was a Viennese zoologist, a minor composer, an amorous lover and a committed socialist. As a biologist, he combined considerable experimental skills with a neo-Lamarckian outlook, to produce a series of investigations on sea-squirts, salamanders, lizards and toads which demonstrated to his satisfaction that physical changes effected by an organism's adaptation to a given environment are "preserved" by heredity and genetically transmitted to its offspring. For Kammerer the crucial experiment involved the sea-squirt (*Ciona intestinalis*), but his neo-Darwinian opponents—based in England and led by William Bateson—concentrated their attention on his results concerning the midwife toad (*Alytes obstetricans*). Ultimately this dispute boiled down to a challenge of Kammerer's integrity as an investigator. When, in the summer of 1926, it was shown that his sole remaining specimen of midwife toad was (or had been rendered) a fake, his antagonists appeared to be vindicated. Shortly afterwards Kammerer committed suicide, an action which effectively discouraged further interest in his work.

Why then has Koestler seen fit to return to this distant controversy? His answer is straightforward: "The secret of (Kammerer's) attraction lies partly in his complex character and tragic fate, but above all in his heretical ideas, that is, Lamarckianism". Since this is a heresy for which Koestler has expressed a guarded sympathy in the past, we might expect him to exhibit some telltale signs of bias.

On the central issue of Kammerer's honesty, however, the author is patently sincere when he argues that "I did not start with the intention to rehabilitate Paul Kammerer, but I ended up with an attempt to do so". Moreover, I believe that Koestler has achieved his immediate purpose. By virtue of diligent reading and of interviews with survivors of the controversy, and an ingenious simulation of the original forgery, he has managed not only to establish his subject's innocence but to provide as well good reasons for performing Kammerer's experiments again. Here Koestler should earn our profoundest admiration.

Unfortunately, the combination of his initial triumph and philosophical presuppositions has placed too great a strain on whatever empathy the author may ever have possessed for the early neo-Darwinians. Bateson and his cohorts are thus depicted as "the defenders of the new orthodoxy" and, even worse, "an inhuman Establishment" whose campaign of defamation was the essential precondition for Kammerer's death. Faced with this description, I would maintain that Koestler has viewed his material through the wrong end of the right microscope.

For example, he is correct to stress the importance of the participants' attachment to dogma but his portrayal of this tendency as "unscientific" reflects an inadequate understanding of the social processes of science. Drawing on the work of Kuhn and others, it is surely evident by now that fidelity to a conceptual paradigm is a necessary concomitant of "normal" scientific research. When a new school of thought attempts to displace an older one, the resulting boundary disputes are bound to be bitter and protracted. For the stakes are not merely intellectual, but also institutional: to the victor will go the spoils of future students and funds for research.

It is in this light that we must examine the reception of Kammerer's work in England. At that time it was classical zoology, not experimental genetics, which constituted the "establishment". Bateson's bastion was indeed a beleaguered one, defending itself along two fronts against statisticians and zoologists. By the 1920s, the generals and lieutenants of the respective armies were battling regularly over such issues as religion, reductionism and eugenics, not to mention neo-Lamarckianism. Whenever a new result seemed to support one side or the other, it was certain to be brandished eagerly and attacked vigorously (most often in the columns of *Nature*). This was the fate meted out to Kammerer, once he was placed in the centre of such an academic maelstrom. Ironically, his defeat did not immediately further the instrumental aims of the geneticists. As late as 1935, it was still possible to count the number of UK professorships and studentships in genetics on one hand; the numerical preeminence of the zoologists was still undiminished.

Lamarckianism, on the other hand, was virtually eliminated from the picture (in Britain). To the lay reader of Koestler's book, this might seem startling, because the author has failed to give a fair comparison of the relative strengths of the two sides in the 1920s. Placed against the achievements of the schools of chromosomal heredity and population genetics, the neo-Lamarckians could only muster a set of highly disputed experimental results. Even on the assumption that their data were correct, they had no plausible (physiological) theory to explain how environmental adaptations could alter the hereditary material. Apparently Kammerer was no exception to this rule.

Thus did a new orthodoxy arise to be transformed triumphantly in a few decades into the new field of molecular biology. Koestler does concede (without sufficient emphasis) that the orthodox have often differed among themselves as to the conclusiveness of the neo-Darwinian synthesis. English left-wing scientists, in particular, have often hedged their bets on this one.

The mention of politics reminds us that theories of heredity necessarily have ideological significance: what kind depends on the socio-historical context in which they are worked out. In nineteenth-century Britain liberals tended to be hereditarians and conservatives talked like environmentalists. About seventy years ago these linkages were reversed. This helps to explain why Kammerer's chief English defender, the elderly zoologist E. W. MacBride, was as far to the right as his Austrian colleague was to the left. As a prominent Bolshevik sympathizer (indeed, because he was one), Kammerer was invited to establish an institute in the Soviet Union. But so too was the geneticist H. J. Muller. Contrary to Koestler, the Russian scientific establishment was not at that time "committed by the party line to the Lamarckian theory of evolution". When Lysenko's school did finally emerge, few Western biologists were prepared to face the political and professional sanctions of espousing any form, no matter how diluted, of neo-Lamarckianism.

Now, in the eighth decade of this century, environmentalism is reasserting itself within the life sciences. Witness the growth of animal behaviour, developmental biology and ecology. Even at the molecular end of the spectrum the faith of an earlier time in Crick's "central dogma" is not quite secure. When these factors are added to a resurgence of organicist philosophy and a revulsion against Jensenism, Koestler expects us to wonder whether neo-Darwinism will be modified by any Lamarckian additions. Koestler envisages just such a possibility. And so we shall PAUL GARY WERSKEY

Newton as Geometer

The Mathematical Papers of Isaac Newton. Edited by D. T. Whiteside. Vol. 4: 1674–1684. Pp. xxxii+678+4 plates. (Cambridge University: London, June 1971.) £18.

EACH new volume of Whiteside's exemplary edition of Newton's mathematical papers adds significant features to the picture we may try to form of this secretive genius. The present volume reveals Newton as a geometer: a third of it (part II) is devoted to remarkable geometrical research, datable from the years 1678–80 and in large part not previously known; another third (part III) reproduces unfinished drafts of treatises on fluxional analysis (about 1680) and computation by series (1684), which cast more light on the essentially geometrical character of the novel conceptions and methods he used in the *Principia,* but only grudgingly and inadequately published as a lemma in the second book of that work. Also in the remaining part of the volume, in which papers of more algebraical or arithmetical content from the decennium 1674–84 are collected, Newton's geometrical turn of mind is apparent, not only in his trigonometrical treatises (of mainly didactic interest), but even in his treatment of Diophantine problems.

Once more the documents (abundantly annotated by the editor with unfailing erudition and shrewd judgment) do justice of silly tales endlessly repeated by scientists lacking historical sense. This time, they expose the inanity of speculations too often expressed about the geometrical style of the *Principia*: how likely indeed that Newton would have deliberately clothed in ancient geometrical garb results of purely analytical computations! As Whiteside rightly points out, Newton's style was thoroughly in the modern tradition initiated in the sixteenth century and given its characteristic expression by the Cartesian school: this tradition built, of course, on the conceptions of the ancient geometers, but it blended them with the algebraic methods which had hitherto been left to develop along their own lines in the hands of practical men. In matters of mathematical thought and style, the innovator was Leibniz, not Newton. The fluxion idea was the most strikingly successful product of this blend of geometry and algebra: the kinematical conception of a curve as a trajectory resulting from the composition of two motions had been revived by the Italians and brought to Cambridge by Barrow; Newton's decisive step was to algebraize it—a step nearly missed by René de Sluse, who was familiar with Torricelli's kinematical method of drawing tangents to curves and also knew in special cases how to derive an algebraical expression for the subtangent from the Cartesian equation of the curve. Newton's success is due to his superior grasp of the algebraical side of the problem, embodied in his method of series expansion. The third part of the volume under review contains in this connexion documents of the highest importance, in which we see Newton endeavouring (not altogether correctly) to answer Leibniz's queries about the universality and completeness of his method. Had these drafts not been put aside when Newton concentrated on the writing of the *Principia,* the later priority squabble might have been avoided, or at least might have taken the more useful course of an objective confrontation of the two rival approaches.

The most surprising items, however, are found in the second part of the volume, among Newton's unpublished papers on geometrical topics. They give us the clue to Newton's motivation for including in the first book of the *Principia* the purely geometrical section V on the construction of conics. It appears that he wanted in the first place to challenge Descartes's boastful assertion that his analytical solution of Pappus's problem transcended the scope of the ancient methods. Indeed, as we now learn, Newton produced a general solution based on simple geometrical reasoning, which he regarded as a tentative restoration of the hidden analyses performed by the ancient geometers. This led him, however, rather naturally to a more general and deeper investigation of the universal characterization of conics: the tract on this subject, reproduced in the volume, and of which only the beginning was inserted in the *Principia,* is a masterpiece which places Newton among the very few geometers of the time who rank as precursors of projective geometry; it shows in fact that he not only recognized the fundamental projective properties of the conics, but explicitly introduced the notion of projective correspondence. The material here made available (the editor promises us more in the same vein for later volumes) allows us to understand the true meaning of Newton's admiration for the ancients: he was better than anyone entitled to appreciate their methods after he had rejuvenated them and given such proof of their latent power. L. ROSENFELD

Power and Environment

Power Generation and Environmental Change. Edited by David A. Berkowitz and Arthur M. Squires. Pp. xxiii+440. (MIT: Cambridge, Massachusetts, and London, 1971.) $16.95.

THIS book is the proceedings of the symposium on "Power Generation and Environmental Change" held by the American Association for the Advancement of Science at the annual meeting on December 28, 1969.

The book is divided into five main sections, beginning with a short discussion on the broad aspects of the main problem: the impact on the environment of the steadily increasing demand for energy coupled with an increasing population. What effects will this have on the quality of our air and water and on the ecology of plants and animals? Two approaches are possible to control harmful effects: the first is to use even more technology to prevent air and water pollution and to recognize that society must bear the cost; and the second is to ration the consumption of energy per head and to limit the increase in population.

The second section deals with nuclear power stations and possible effects of radioactive releases on public health and safety. It discusses only light water reactors, of the boiling-water or pressurized-water types, and gives some data on the radionuclides released in the liquid effluent and gaseous emission. As far as gaseous emissions are concerned the pressurized water reactor in normal operation produces even less than a coal-fired power station, which it is agreed presents a negligible hazard. The emission from a boiling water reactor is, however, at least four orders of magnitude greater. Several contributions discuss the relation between radiation dose and cancer, the possible genetic consequences, and the radiation dose limits which should be adopted to reduce such risks below "natural" or other more familiar risks. It is here that there is the greatest controversy, and estimates by different authors of a radiation exposure situation vary by a factor of up to 10,000.

Hydroelectric generation and pumped storage systems, discussed in the third section, need have no adverse overall effect on the environment, and in fact often make it possible to provide improved facilities to enjoy the countryside. Nevertheless the author of the contribution on ecological effects paints a frightening picture of "a sepulchral forest of submerged trees", and "a man whose home is drowned, whose form of livelihood is interrupted, whose urine turns to blood, whose eyes go blind, or who shakes with malaria because a lake was created".

The fourth section is devoted to power

generation from fossil fuels, coal and oil. The main environmental problem is to reduce the effects of sulphur dioxide, either by dispersion using tall stacks, or by limiting the emission by removing the sulphur from the flue gases at the power station, or from the fuel oil at the refinery. The climatic consequences of the accumulation of carbon dioxide in the atmosphere are discussed, and there are some interesting contributions in the new field of atmospheric chemistry—the study of "photochemical smog", and the life cycles of sulphur dioxide and nitrogen oxides on a continental or a global scale.

The final section on "waste" heat is disappointing. There is far too much repetition; the same basic information is presented many times with variations which must confuse the non-specialist reader. For example, "nuclear plants require 40 per cent more cooling water than fossil-fuel plants" (p. 345); "nuclear plants waste 60 per cent more energy than fossil-fueled plants" (p. 353); and "fossil-fuel plants discharge approximately one-third less waste heat to the cooling water than do nuclear plants" (p. 369). In only one instance is it pointed out that future designs of nuclear plants will not require more cooling water than fossil-fuel plants. Two of the authors use the term "thermal pollution" for warm water discharges and emphasize the possible deleterious effects and the need for the control of temperature rises to a few degrees (F). The other contributors to this section take a more constructive approach and point out that the problem can be solved by the proper siting of power stations and the design of cooling systems, and that beneficial uses of "thermally enriched" water can be developed.

Summing up, the book is rather a mixed bag, but the patient reader can assess the various contributions for himself and obtain an overall picture of the American environmental scene—which, of course, is not necessarily relevant in Britain.

J. S. FORREST

Invertebrate Fossils

Atlas de Paléontologie des Invertèbres. By René Verniory. Pp. 217+89 plates. (George Librairie: Genève; Masson et Cie: Paris, 1970.) 190 francs.

THIS volume has been published after the author's death. The wholly laudable desire to ensure that the dead man's work has not been in vain cannot gloss over the real difficulties involved. Most of the deficiencies of the book can be ascribed to this.

The plan of the book is one which I have met before in works published in Switzerland. It consists largely of a systematic summary of the salient facts about the palaeontology of the invertebrate phyla, these being illustrated by sketch diagrams on fold-out sheets. These fold-out illustrations make up about half the thickness of the volume.

The criticisms of the book—understandable under the circumstances of publication—are: failure to cover some invertebrate groups at all; a sometimes obsolete classification—it has been known since the work of Kozlowski in 1938 that the graptolites are not coelenterates—and an utterly inadequate bibliography. For these reasons the work cannot be considered as a standard work of reference and its price would, I think, effectively prevent its sale in England for any other reason. It is clear why the book is so expensive—the cost of the many fold-out pages must be high. This does not alter the hard fact that only an indispensable reference work—the *Traité de Paléontologie* itself is an example—can hope to have a sale when its price is more than £20.

K. A. KERMACK

Cancer of the Lung

Morphology of Experimental Respiratory Carcinogenesis. Edited by P. Nettesheim, M. G. Hanna, jun., and J. W. Deatherage, jun. (Proceedings of a Biology Division, Oak Ridge National Laboratory, Conference held in Gatlinburg, Tennessee, May 13–16, 1970.) Pp. xiv+483. (National Technical Information Service, US Department of Commerce: Springfield, Virginia, 1970.) $6.

THIS book covers the proceedings of a conference which was a logical sequel to one held in 1969 and reported in the *AEC Symposium Series* No. 18. The earlier meeting concentrated on methodology whereas the papers given at the 1970 symposium, although they still include a considerable amount of experimental detail, lay the main emphasis on the resultant lung changes as seen by light and electron microscopy. This has been supplemented in some cases by histochemical studies.

The experimental species used by different authors vary from the usual laboratory rodents to the white Pekin duck, thus there must be considerable variation of normal lung structural detail. Nevertheless a useful if fairly generalized synopsis of the main cell types found in respiratory tissue is given with some histochemistry. The study of cell kinetics is limited to rats and mice.

Although the bulk of the material concerns experimental oncogenesis, there are also papers on human occupational hazards which may lead to cancer of the respiratory tract. Particular reference is made to the uranium mining and asbestos industries and the influence cigarette smoking may have on individuals exposed to these hazards. Much evidence supports the idea that the induction of respiratory cancer can be multifactorial and such a possibility has not escaped the notice of the scientists, a number of whose experiments are designed to examine this facet of the problem.

Many of the investigations are to establish biological models for the future evaluation of changing (and it is hoped, improved) environments either natural or industrial; others are attempts to elucidate the mechanisms by which a particular carcinogen acts. It is important therefore that there should be uniformity of nomenclatures and a description of the WHO classifications of human lung tumours is given. In the later "Panel Discussions" some tentative ideas are put forward for similar but less detailed classifications of natural and experimental animal tumours. It is certain that the majority of experimentalists will welcome this move and the project is being continued by the International Agency for Cancer Research at Lyon.

This is a book essentially for those actively involved with the problem of experimental respiratory carcinogenesis to whom it is well recommended. Some of the work reported is not entirely new but many of the papers are by recognized world authorities in this field of research. These proceedings therefore make interesting and informative reading as well as being a useful source of reference material in this still rather disputatious area.

BRIAN R. DAVIS

Hydrogen Bonding

Hydrogen Bonding. By Serge N. Vinogradov and Robert H. Linnell. Pp. xi+319. (Van Nostrand Reinhold: New York and London, July 1971.) £4.75.

THE aim of this book is to review hydrogen bonding and the many and important applications of this phenomenon. The book is stated to be written particularly for undergraduates and postgraduate students and research workers in the life sciences. Because of the breadth of topics and wide range of experimental techniques that are used in studying hydrogen bonding, this is not an easy task to undertake.

In my opinion, the concept of the book is admirable and timely. In addition, with a few exceptions, the balance of topics chosen for the different chapters is also very good. However, the book falls down very seriously in execution and contains an unusually large number of errors. For example, the very first figure, Fig. 1-1, is wrong, Fig. 1-4 is poorly and inaccurately drawn, and Fig. 2-1 is also wrong. Such rather obvious mistakes which occur at the beginning of the book are also to be found not infrequently in later chapters. Another example is given by the first paragraph in section 2-7 where the changes in molar volume that can be correlated with hydrogen bonding are discussed in a confused manner. This is so much so as to give the impression that the phenomena concerned are quite different in organic chemistry and in inorganic chemistry! Again, on page 50 it is stated that "The force constant k is . . . directly proportional to the frequency (ν) and indirectly proportional to the square root of the reduced mass . . .". This statement is in contradiction to equation (3-2) on the previous page. Also on page 50 the diagrams of the vibrations of a water molecule are crudely and partly incorrectly drawn. Because of errors of this type the book cannot be recommended for basic teaching purposes. The problems set at the end are rather repetitive in type, mostly involving equilibria deduced from spectroscopic measurements.

Nevertheless the balance and coverage of the literature are good and the book will undoubtedly be useful to many more expert scientists who will be pleased to see the salient aspects of the subject spelled out, and who are not likely to be put off by the errors scattered about. I have the impression that the book has been written in too much of a hurry and as a result is of much lower standard of execution than it ought to be. Nearly all the errors noted would almost certainly have been corrected if the authors had asked experts in the subject-matter of the various chapters to read and comment on them before printing. It could still be worthwhile to do this for a possible later impression.

N. SHEPPARD

Dyes and Pigments

Colour Chemistry. By R. L. M. Allen. Pp. xii+336. (Thomas Nelson and Sons: London, 1971.) £5.

FOR several years there has been a need for a modern introductory textbook on colour chemistry, and this work by R. L. M. Allen is the second book to appear in the last three years intended to fill this gap. The author has indicated that the book is presented as an introduction both for specialist colour chemists and for students whose main interests lie in related branches of pure chemistry or technology. Consequently a comprehensive coverage of the field has not been attempted, and the reader is frequently referred to the more specialist literature where a deeper treatment is required.

The development of the subject-matter of the book follows well established lines, and after introducing the reader to the physical basis of colour and the history and classification of dyes, subsequent chapters deal with classes of dyestuffs largely according to their chemical constitution. Pigments are briefly dealt with, and to illustrate the less obvious applications of colour chemistry, chapters on fluorescent brighteners and colour photography are usefully included.

It is obviously very easy to criticize the content of a book of this type, since the selection of material is very much a matter of personal choice. Generally, however, the field has been well covered, and the more obvious omissions that have been made, for example the intermediates of dyes and pigments, do not detract from the value of the book. Perhaps a more serious omission is the absence of a discussion of the mechanistic principles of diazotization and coupling, two of the most important processes of colour chemistry. The theoretical treatment of colour and chemical constitution is brief but adequate for a book of this level, but surprisingly few practical examples of empirical colour relationships are given. The new student is given little indication of the position and type of auxochromes necessary to give, for example, red monoazo dyes, or blue anthraquinone dyes.

The author has succeeded in presenting material relevant to modern colour chemistry, largely by drawing on his own industrial experience and by frequent reference to the recent patent literature. The latter is commendable in a field where disclosures of important technological developments often only occur many years after their introduction. One criticism concerns the brevity with which disperse dyes are treated by comparison with dyes for natural fibres, which does not reflect the true technological importance of the former dyes at the present time. A heavier emphasis on disperse dyes for synthetic fibres, perhaps at the expense of azoic and direct dyes, would have presented a more accurate picture.

This is a readable, well presented book which will provide the reader with a useful, up to date background to colour chemistry.

J. GRIFFITHS

Fish Adaptation

Explorations in the Life of Fishes. By N. B. Marshall. Pp. 204. (Harvard University: Cambridge, Massachusetts; Oxford University: London, October 1971.) £2.30.

A SERIES of lectures given at Harvard in 1963, and refurbished in 1964 and in 1967–8 for the Universities of British Columbia and of Miami, is at last published in revised form. The revision must have been thorough, for a large proportion of the bibliographic references are (as one would hope) subsequent to 1963.

Marshall's *The Life of Fishes* was published in 1965, during the gestation period of this book (and it may well be that publication of this book was delayed for that reason). The two books are, however, very different. The earlier one was large, comprehensive in scope, and apparently intended to be accessible to the lay enthusiast as well as to professional zoologists. The new book is smaller, more selective and seems to assume substantial ichthyological knowledge in its readers, who are expected to be familiar with the wide variety of fishes cited as examples and to be enlightened by remarks such as "one has only to think of the gobies". There is an appendix which deals briefly with the classification of teleosts, but this will not be much help to the novice, particularly as it is unillustrated and includes no references to illustrations of fishes elsewhere in the text. Technical terms such as "hypural" and "stenobathic" are used without definition and the reader is expected to be able to fill in for himself the explanations behind statements such as "Yet a large swimbladder has disadvantages: for the greater its capacity, the more effort a fish must exert to keep station after a given rise or fall above a level of equilibrium".

The book has three main sections. Chapters 1 and 2 discuss the success of teleosts and some features of their design for swimming. Chapters 3 and 4 are about the specializations of deep sea teleosts and chapter 5 is a long discussion of convergent evolution. The discussion of success is extremely interesting, though some of the main arguments are only sketched out. The section on deep-sea teleosts is especially welcome on account of Marshall's unrivalled knowledge in this field. The section on convergent evolution overlaps rather awkwardly the section on deep-sea fishes; the eyes, lateral lines and swimbladders of deep-sea fishes are discussed in both sections and there is even a part of the convergent evolution chapter specifically about convergences of deep-sea fishes. I would have found this chapter more interesting if fewer examples of convergences had been considered and the space so saved used to show in a few cases precisely why it is believed that certain resemblances are due to convergence rather than to common ancestry.

The book is illustrated by line drawings which are apt, informative and attractive, but are sometimes rather too small for comfortable study. This is because the text has been set up so as to fill only two-thirds of the width of each page, and most of the illustrations have been squeezed into the margins.

This is a stimulating book and I am glad to have my copy, but it would be more generally useful if it had been written with more thought for the reader who may be a sound zoologist but is not particularly knowledgeable about fishes.

R. MCNEILL ALEXANDER

CORRESPONDENCE

Insecticides

SIR,—Worthington (*Nature*, **234**, 55; 1971) states positively that "the proposed banning of DDT in the USA will stimulate the search for better insecticides and integrated pest control . . ." and the "efforts in these directions remain at a relatively low ebb so long as the bludgeon of DDT and other persistent synthetics is readily available". His argument was somewhat damaged by your footnote. Also, his premise is the reverse of the obvious facts; the success of DDT was a great boost to the search for other and better insecticides, just as the success of the Ford car triggered competition in the automobile industry. Many millions of dollars were spent in insecticide research in the past two decades and the stimulus for the expenditure was reinforced by the onset of resistant strains. The WHO has tested more than 1,400 new insecticidal compounds since 1960 for suitability in vector control of malaria.

The use of pesticides has furnished bread, and now the attack on them provides circuses. Contrary to Worthington's reasoning, several large organizations that searched for new insecticides are weary of being pursued by environmental lions ("a public relations headache"), and are leaving the Colosseum (*Chem. Eng. News*, 16, 1971). For example, Standard Oil of New Jersey has put its pesticides research programme up for grabs. If new insecticides are needed for integrated control, how long would it take to "clear" one—five years? Almost any substance will produce tumours, or deformations in embryos, if enough is injected, and there is always the question of "long-term effects" which are too subtle to detect, but not too subtle to be used in arousing fear of the unknown.

Yours faithfully,

THOMAS H. JUKES

University of California,
Berkeley

Arms Control

SIR,—Ralph Lapp ends his review of the "Impact of New Technologies on the Arms Race" (*Nature*, **234**, 273; 1971): "The United States appears to be racing itself, not competing with the Soviet Union, as it seeks to exploit military technological opportunities."

He seems to be implying that the United States *alone* is arms racing (rather than that the form of US arms racing does not relate to the form of Russian arms racing). The present situation surely is that while both superpowers continue to proliferate nuclear weapons, the Soviet Union has already substantially overtaken the United States in numbers of ICBMs, in megatonnages, and in underground tests of large nuclear devices; that the Soviet Union is approaching parity with the United States in missile launching submarines, has already flown a new supersonic long range bomber, has long since had an ABM system deployed and an Orbital Bombardment system, and now has a non-nuclear anti-satellite capability as well.

As one who believes, passionately, that arms control and disarmament are a necessary (though not sufficient) condition of human survival, my heart sinks every time an American dove proclaims his belief that today the United States alone is arms racing or exporting weapons or whatever. This was indeed virtually so when many of today's doves were working with the Kennedy administration, but it has not been the case for the last half decade or more: is it not time they recognized that today the Soviet Union is acquiring and proliferating weapons of all sorts at least as vigorously as the United States then did?

Yours faithfully,

ELIZABETH YOUNG

100 Bayswater Road,
London W2

Ocean Conservation

SIR,—The terrestrial environments of the Earth have been divided by ecologists into a series of "biomes", according to variations in climatic and geophysical factors. Within these biomes, a large variety of different types of habitat have been recognized, each with more or less distinct floral and faunal characteristics.

The oceans of the world, which cover 70.8% of the Earth's surface and contain 80% of known living organisms, can also be divided into distinct regions, according to climate and depth. These regions have distinct faunal and floral characteristics, as do the terrestrial biomes, although the distinction is considerably blurred by the activity of the ocean currents and mixing of separate water bodies.

Nearly all nations now have devoted thought and effort to conservation of their natural resources by the establishment of parks, reserves, sanctuaries and so on, setting aside areas for research, education and recreation. A question now occurs to me. What steps are being taken to do the same for the marine habitats?

The Annual Report of the President to the Congress of the United States of America on Marine Resources and Engineering Development in April 1970 gives a brief but good summary of marine pollution. But throughout the report, the ocean is referred to in the singular. Further on, the same report mentions that many countries are taking steps to set up conservation areas in their coastal waters. Coastal environments are distinguished as estuaries, lagoons, beaches, wetlands and so on. Some countries have established underwater marine parks inside their territorial waters. Should not the open oceans be recognized as a series of environments, each worthy of some attempt at conservation?

With the fast developing technology of marine mining and underwater engineering, the declaration of protected areas in the ocean should not be left too late. Benthic faunas in particular would suffer in large scale dredging and boring operations. So far, open ocean conservation has consisted of the protection of single species from overexploitation. Terrestrial conservationists have found out that preservation and management of environment is a better approach.

There are tremendous problems associated with the setting-up of open ocean protected areas, different from those faced by terrestrial conservationists. A few spring to mind. (1) Which areas to choose? This is relatively simple, and can be solved by present surveying methods, if enough time is available. (2) Who would control the proposed areas? Because they would in most cases be outside territorial limits, the responsibility would fall to the UN. Costs should be shared by the member nations of the UN. (3) Management problems, such as counteracting pollution by contamination from outside, would arise. These are some problems, but it must be agreed that attempts must be made to set up these areas, and research into management methods must be worthy of attention.

Yours faithfully,

JAMES MILLER

University of San Carlos,
Cebu City,
Philippines

Obituary

Dr Jean Nitsch

On June 28, 1971, Dr Jean P. Nitsch died on the Brittany coast while diving to study marine plants. It was typical that his zest for observation and inquiry should lead him into new and unfamiliar techniques, and his death, at 49, has robbed France and plant physiology of a very versatile investigator.

Born on September 15, 1921, Nitsch's career was divided between his native France and the USA where he was equally at home and as well known. As in the case of most of his generation the Second World War interrupted his Baccalaureate studies, but in due course he acquired diplomas in France from the University of Grenoble (1943), the Sorbonne (1946) and as Ingénieur Agronome de l'Institut National Agronomique de Paris (1947). But it was his association with Professor F. W. Went at the California Institute of Technology, Pasadena, which culminated in a doctorate awarded in 1950, that first brought him to the attention of the scientific world. The title of his thesis, *The Role of Plant Hormones in Fruit Development*, indicates the trend of Nitsch's work throughout. He was dedicated to the interpretation of the controls of growth through chemical regulation and strongly motivated to work in areas beneficial to horticulture.

Even before the presentation of his thesis Nitsch's work became known because of his attempts to culture immature fruits aseptically, *in vitro*, and early papers appeared both in France and in the USA[1–3]. In this early work a favourite experimental material was the multiple strawberry fruit, and Nitsch drew attention to the role of achenes in the development of the receptacle and of auxin (IAA) in the growth and morphogenesis of the strawberry. From this starting point Nitsch moved rapidly to the culture of excised ovaries, to the general use of proliferated callus cultures in the study of growth, and to a variety of investigations concerned with the role of hormones in sex expression and the development of fruits[4,5]. His interest in these fruits was maintained at Harvard (1950–51) as a postdoctoral research fellow and, after a brief return to France, at Harvard again as a research fellow (1953–55) where he worked in the laboratory of, and was influenced by, Professor R. H. Wetmore.

From 1955 to 1958 Dr Nitsch was an assistant professor at Cornell University and was in charge of a course on plant physiology applied to horticulture. His role in the Department of Floriculture at Cornell allowed him to exploit his interest in the use of aseptic culture procedures, while he also interested himself in the problems of plant propagation, in photoperiodism, and in the chemical induction and regulation of growth.

After returning permanently to France in 1958 Nitsch was associated (in obvious continuity with his experiences at Pasadena) with the development and use of the Phytotron, a large installation for the environmental control of the growth of plants, at Gif-sur-Yvette near Paris, and he served as deputy director there from 1958–62. It is in this capacity and successively as Directeur-Adjoint d'Institut de Recherche au CNRS (1962–69) and as directeur du Laboratoire de Physiologie Pluricellaire from 1969 until his death that Nitsch's scientific stature came to be recognized internationally. Some 35 investigators from 16 countries were attracted to the Phytotron during the years of his association with it. Nitsch was also appointed to an academic position in France as professeur à l'Institut National Agronomique in a chair designated for plant physiology.

In conclusion, certain areas of Nitsch's wide range of interest may be mentioned. The early work on auxin and growth promoting substances prompted him to show by chromatographic means that many naturally occurring substances had auxin-like activity. This interest was to make him a welcome participant and contributor to a succession of international conferences on plant growth regulating substances. Nitsch contributed to the conference held at Wye, Kent, in 1955[6], and the maintained interest in chemical regulation of plant growth led him to organize a similar international conference at Gif, the proceedings of which were published in 1964 under his editorial supervision[7]. Any full current treatment of the chemical controls of growth must note Nitsch's work on cell division or cell enlargement, using a variety of assay systems and as brought about by a variety of substances. His work has involved auxins, cytokinins, gibberellins as well as substances and extracts held to be more specifically associated with flowering[8,9].

In logical continuation of Nitsch's interests in aseptic culture of somatic tissues and floral organs, he intervened most effectively in the culture of haploid cells from anthers of tobacco[10] and studied their development into haploid plants. By subsequently doubling their chromosome numbers, Nitsch obtained, in this way, completely homozygous plants from certain mutant forms and published in this field earlier this year[11]. Nitsch's published work includes at least 154 papers and a number that will appear posthumously.

No reference to Jean Nitsch would be complete, however, without tribute to his friendliness and the hospitality that he and his wife, Colette, extended to so many scientific visitors to France, his laboratory, and his home in Gif. He is survived by his wife, Dr Colette Nitsch, and by two children.

[1] *CR Acad. Sci., Paris*, **229**, 445 (1949).

[2] *Science*, **110**, 499 (1949).

[3] *Amer. J. Bot.*, **37**, 211 (1950).

[4] *Quarterly Review of Biology*, **27**, 33 (1952).

[5] *Ann. Rev. Plant Physiology*, **4**, 199 (1953).

[6] In *Chemistry of Plant Growth Substances* (edit. by Wain, R. L., and Wightman, F.), 3 (Butterworths, London, 1955).

[7] *Régulateurs Naturels de la Croissance Végétale* (edition du Centre National de la Recherche Scientifique, Paris).

[8] *Ruhland Handbuch der Rflanzenphysiologie*, **15** (**1**), 1537 (1965).

[9] In *Plant Physiology: A Treatise* (edit. by Steward, F. C.), **6A**, 403 (Academic Press, New York City, 1971).

[10] *Science*, **165**, 85 (1969).

[11] *Pollen Development and Physiology* (edit. by Heslop-Harrison, J.), 234 (Butterworths, London, 1971).

Announcements

University News

Professor Thomas H. B. Symons, president and vice-chancellor of Trent University, Ontario, has been elected chairman of the **Association of Commonwealth Universities** for 1971–72. **Sir Charles H. Wilson**, principal and vice-chancellor of the University of Glasgow, has been elected vice-chairman and **Sir Douglas Logan**, principal of the University of London, honorary treasurer, for the same period.

Mr R. W. Beard, King's College Hospital Medical School, has been appointed to the chair of obstetrics and gynaecology tenable at St Mary's Hospital Medical School, **University of London. Dr G. Hamilton Fairley**, Imperial Cancer Research Fund Medical Oncology Unit, has been appointed to the Imperial Cancer Research Fund chair of medical oncology tenable at St Bartholomew's Hospital Medical College, and **Mr J. H. Sowray**, King's College Hospital, has been appointed to the chair of oral surgery tenable at King's College Hospital Medical School.

Miscellaneous

Dr R. D. Cannon, University of East Anglia, has been awarded the first **Butterworths scientific fellowship for authors.** He will take up the fellowship in 1972 to write an advanced monograph on electron-transfer reactions.

Nominations are requested for the **Lewis Rosenstiel award for distinguished work in basic medical research,** which will be made in the spring of 1972 on the basis of the recommendation of a panel of outstanding scientists in the field. Preference will be given to recent discoveries of particular originality and importance. Further information is available from Dr H. O. Halvorson, director of the Basic Medical Sciences Research Center, Brandeis University, Waltham, Massachusetts 02154, USA.

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Agenda for Strathclyde

Public discussion of the Dainton and Rothschild reports has so far been more of a whispering campaign than a debate. Among academic scientists, there are frequently to be heard fierce expressions of scorn for Rothschild, but there has so far been no convincing demonstration that university scientists are aware that the time has arrived when some change in the organization of British scientific research would be appropriate. Most university opinion appears to be Daintonite—"I'm for Fred" has become the slogan but few people acknowledge the existence of the forces which have compelled a re-examination of the organization of British science at this point. But academic scientists are only the tip of the iceberg. So far, nothing has been heard of the opinions of those who are much more directly concerned—the chairmen of the research councils, the directors of research council laboratories and even the people who work in them. The trouble is, of course, that civil servants are prevented from speaking out in public. This at least is the convenient supposition of those who are afraid to burn their fingers. This is why a conference which the Council for Scientific Policy has arranged next week at Strathclyde should be an opportunity for flushing out the views of those who have so far been much quieter than they should have been.

To begin with, it is essential that the scientific community as a whole should recognize the reasons why the Dainton and Rothschild reports have appeared at this time. The tale goes back to the late 1960s, when it became apparent that the research councils had become an exceedingly mixed bag. The research councils concerned with science and social science were largely handmaidens of higher education, and although the Science Research Council is right to complain vigorously if its industrial connexions are overlooked, the truth remains that its existence is justified chiefly by the way in which it provides grants for university research and stipends for university research students. Although the Science Research Council has quite properly sought in the past few years to make researchers work on problems which are likely to bring industrial benefits and research students more willing to take jobs in industry, the ways in which it spends its money contribute only indirectly to industrial innovation. The arguments given by the Medical and Agricultural Research Councils in justification of their continued existence are, right or wrong, quite different in style. The Agricultural Research Council is justifiably proud of the benefits which British agriculture has won from such developments as the new strains of wheat which have become available in the past few years. And the Medical Research Council takes the view that there is a long term connexion between the kind of work which it sponsors and the health of the community which pays for the research programme. Only the Natural Environment Research Council lacks a coherent justification and that is hardly a defect to be laid at the doors of those who now administer that shaky organization, which was conceived too rashly in an appendix to the Trend report on research organizations nearly a decade ago, and then sanctioned much too lightheartedly.

Who can be surprised that it should have become increasingly hard to accommodate these different organizations within the same framework as the annual expenditure has grown to a total of £125 million? Seen from the point of view of any government, there must, for example, be serious practical problems in determining how much money should be allocated to the five research councils. If the chief justification of the SRC and of the SSRC is to stiffen the back of higher education, then their expenditure should somehow be linked with the scale of higher education as a whole. (One of the most serious errors of the past few years has been the attempt by two successive governments to breathe life into the polytechnic system without providing a commensurate increase in the funds available to the research councils for the sponsorship of research.) If, by contrast, the Agricultural and Medical Research Councils justify their existence by the practical results which their work will eventually bring, it is only proper that governments should ask whether these results are beneficial, whether the benefits are worth their cost (as estimated by the research councils) and whether it might not be prudent public policy to postpone them. The most sanguine supporter of the principle of autonomy for the research councils will be forced at Strathclyde next week to confess that these questions have not been asked in any pointed way of the Medical and

Nature in 1972

From the beginning of 1972, copies of the Friday edition of *Nature* destined for subscribers in North America, South America, Australia and Japan will be printed in the United States at the William Byrd Press, Richmond, Virginia. Reproduction will be from film flown each week across the Atlantic, which means that all copies will be identical. One advantage of this arrangement is that the subscription price in North America will not be affected by the dollar devaluation.

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The *Nature* index will in future be published once a year in cumulative form, covering all three editions of the journal. The index for 1971 will be sent to subscribers who have ordered it early in 1972. This and future editions will be generated and sorted by computer.

Agricultural Research Councils in the past few years. Instead, their budgets, which have grown much more quickly than that of the Science Research Council, have been determined by much more arbitrary considerations —the increasing cost of research, the specific plans of research directors and general expressions of belief that research in some new field will bring practical results in due course. It is disingenuous of those who now reject Lord Rothschild's doctrine of the consumer/contractor relationship to pretend that the system can continue without some alternative mechanism by means of which governments can apply objective tests to the claims of the research councils that their work is of practical benefit. Because the Medical and Agricultural Research Councils are those which have in the past justified their work in terms like these, it is natural that they should now be the prime targets for the Rothschild reorganization.

The weaknesses of the out-and-out Daintonite position are, in short, that it does not acknowledge that Rothschild has an excuse, let alone a case, and that it supposes that the present organization of the research councils approximates to perfection. Paradoxically, the defence of the research councils would be easier if these matters were openly acknowledged. It would also be helpful if the conference at Strathclyde could decently but publicly bury the notion put forward by Sir Frederick Dainton's working group that the future policy of the research councils could usefully be determined by a board of bigwigs which would, for one thing, be too large to be workable and which, for another, would be so loaded with vested interests (not to mention the President of the Royal Society) that it would probably be locked perpetually in internal conflict. The notion that such a body should be interposed between the research councils and the government department which supports them, the Department of Education and Science, is badly thought out and should be abandoned.

Clearing the decks in this way will make it much easier for the scientific community to attack the Rothschild report at the places at which it is weak—the supposition that government departments could be so well provided with scientific advice that they would become intelligent customers for the work which the research councils are able to carry out. If there is some truth in the belief that many research council laboratories are less good than the best, it is beyond dispute that most government departments, with the possible exception of the Ministry of Defence, are scientifically naive. To be sure, there is a complicated hierarchy by means of which scientific advisers are empowered to put an oar in the water from time to time, but most ministries appear to regard this kind of advice as something between a nuisance and a lucky dip. The notion that scientific inquiry should be an indispensable tool for the attainment of a ministry's political and administrative objectives is still regarded in the civil service as outlandish. The Department of Trade and Industry has inherited from the old Ministry of Technology an apparatus for making interventions in the industrial sector, but this is not a strictly technical matter and, in any case, there are serious doubts about its effectiveness. For reasons like this, the most serious objection to Lord Rothschild's proposals is that they may in present circumstances be outrageously idealistic. Who can be certain that the department would not seize on what he has to say as a licence to commission research and an opportunity for putting in charge of their part of the commissioning process a couple of ambitious principals with two or three years to spend on the way to some more exalted posting? Lord Rothschild acknowledges in his report that his system can only function if the departments are indeed equipped to ask discerning questions of the research councils. It is very much an open question whether this is possible, let alone likely. It follows that the scientific community would be best advised to insist that any radical change of the kind outlined in the Rothschild report should be preceded by a demonstration that this weak link will work.

Another weak point in the Rothschild argument is its indifference to the scale on which money would be spent under the new dispensation. It is all very well to say, as the report does, that estimating the proper size of the science budget is the most difficult task of all but it is irrelevant to the framework within which research is carried out. The truth is that the money questions are important questions. In agriculture, for example, if it is proper that the Agricultural Research Council should spend more than £15 million a year for the sake of benefits to be won, might it not be that twice as much benefit would accrue by spending £30 million a year? Lord Rothschild would say that this kind of question can only be settled empirically, by seeing how eager intelligent customers are to have their questions answered and how much they are willing to pay for the privilege but that, alas, is an argument that stands up only in strictly commercial circumstances. The difficulty running through the question of how governments should support research in the civilian field is that governments are consistently unclear why they spend money on these activities at all. Sometimes they argue (as British governments did in relation to the cooperative research associations throughout the 1940s and 1950s) that the government's job is merely to set an example to private organizations. Sometimes governments argue that they must undertake the research that other people will not touch (which is an argument running counter to the Rothschild doctrine). Sometimes they argue that in fields such as agriculture and medicine (but not, paradoxically, in telecommunications), research is an indispensable part of industrial strategy which no government can afford to see neglected. Whatever the supposed motivation of expenditure on civil research, however, it remains a simple truth that governments spend in one year an amount of money defined first of all by the need that it should not be very different from what they spent in the previous year. In present circumstances, for example, it would be quite possible for the British government to say that the opportunities for medical research springing from recent discoveries with cancer viruses are so promising that extra money should be spent on work like that. But the Department of Health and Social Security has been conspicuous by its silence on the subject. The chances are that in a tight year for the economy, no government department will have the courage to argue the case for more expenditure, however beneficial the outcome might be. And the accumulation of decisions and indecisions like this probably ensures that, as the years pass, the scale of public expenditure on civil research is much lower than it should be.

Underlying the supposed opposition of Rothschild and

Dainton—and in reality, the two documents have more in common than first meets the eye—is the assumption that whatever framework is eventually evolved for the channelling of public funds to civil research, the final decision will be made in confidence, by government officials or members of the research councils sworn in advance to secrecy. Over the past few years, it has become apparent that the habit of secrecy has been one of the most serious weaknesses in the apparatus of the research councils. It is true that the Science Research Council in particular, and the Medical Research Council to a lesser extent, have built up elaborate networks for giving advice on the expenditure of money, but this does not entirely dispose of the fear that all of these organizations would be much sharper, and by extension more productive, if they were more ready to encourage public discussion within the scientific community of important policy issues. The Rothschild recipe would necessarily be still less open to opinion from outside. It would be timely if the meeting next week at Strathclyde were to pay some attention to the question whether these are circumstances in which the fullest benefits may be won from the opportunities created in the past few years not merely in agriculture, medicine, on the continental shelf and in the social sciences but also in important fields of industrial research such as computers, data processing, telecommunications and transport. Scientists are fond of saying that war is too important to be left to generals. Is there not a possibility that science is too important to be left to the scientific advisers? What this implies is that the conference at Strathclyde would be well advised to broaden its sights so as to open the wider question of how best to exploit science for the national and even international good. It will be noticed in passing that the Rothschild recipe says nothing about the role of science in higher education, in civilian industry and in defence.

The Duke and ZPG

In the past fifteen years, the Duke of Edinburgh has enlivened British life in several ways. He has been outspoken about the British press and doubts still linger whether it was he who sprinkled photographers with water at the Chelsea Flower Show. He has been and is still a powerful supporter for the noble cause of the conservation of mammals in Africa. In his time, he has upbraided British industry for failing to make the fullest use of the technology at its disposal. More recently, and perhaps too trendily, he has taken to echoing some of the wilder statements about the future of the British environment. Just before Christmas, he committed himself somewhat tactlessly to the common but mistaken belief that the British population is well on the way to becoming intolerably large. The complaint, of course, is that it is now much harder than it used to be in the 1930s for people to make their way to the beaches in the summer, that city streets are more crowded than they have ever been and that there are many circumstances in which it seems as if the pressure of industry on the environment has sacrificed important amenity. Because people are almost always associated with these developments, it is natural that the growth of population should be blamed. The trouble is that the analysis is mistaken and that population growth is merely a scapegoat.

In the first place, it is important that the number of births each year in the United Kingdom has been falling steadily since the mid-1960s. At the peak, in 1966, there were 980,000 births. In 1970, the number of births had declined by almost ten per cent. It is true that in the years immediately ahead, the post-war bulge may bring about an upward trend, but this could well be compensated for by a decrease of fertility. So why does the population of the United Kingdom continue to increase? Two years ago, the Government Actuary was estimating that the population would have grown from 56 million at present to 59.3 million in 1980, 63 million in 1990 and 68 million by the turn of the century, but he has since been forced by more recent trends to lower his sights. Whatever the uncertainties, however, there is no doubt that the most important single reason for the growth of population in countries such as Britain is the continuing reduction of mortality among adults. Of the extra 12 million people likely to be alive at the turn of the century, nearly three-quarters will be people of working age or those who have retired. If progress in the treatment of cancer and heart disease is as fast as some people hope, the population could grow still faster but all the extra increase will consist of middle-aged people. This is why those who complain (as the Duke of Edinburgh was doing) at the growth of the British population should be required first of all to recognize that the increase of which they complain consists largely of older people. Do they seriously bemoan increased longevity? And although there is a case for thinking of the use of taxation for restraining fertility in developing countries, what reason is there to think that such devices would have that effect in present circumstances in Britain and similarly developed countries? Might it not be more constructive to explore instead schemes for helping people stay at work beyond the ages now considered proper for retirement?

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100 Years Ago

Dr. Hoy, in a paper read before the Wisconsin Academy of Sciences, Arts, and Letters, remarks, in reference to the mammals of Wisconsin, that the elk existed in that State as late as 1863, but is now probably extinct. The moose is still found in considerable numbers. The last buffalo was killed in 1832. Antelopes were also found in Wisconsin in the time of Father Hennepin, although now, of course, driven far to the west. Most of the wild animals are diminishing very rapidly in number, the panther and deer being almost exterminated. The otter and beaver, however, are very persistent. The last wild turkey was killed in 1846 near Racine.

From Nature, **5**, 191, *January* 4, 1872

OLD WORLD

COUNTRYSIDE COMMISSION

How to Run the Parks

THE appointment of a permanent director of the Countryside Commission and the administration of national parks within the proposed new structure for local government are singled out for special comment in the commission's report for 1970–71 (HMSO, £0.68). The decision to build up a management team under a director, Mr R. J. S. Hookway, is regarded by the commission as a positive step forward because it gives the commission its first badly needed permanent senior staff.

During the year, the commission successfully suggested to the Department of the Environment that "progress in accomplishing the purposes of national parks" should be reviewed and plans drawn up for the future. A review body under Lord Sandford was duly set up in July this year and, after visits to all the national parks and several public hearings, it is expected to report by the end of 1972. The commission was, however, also acutely aware that its views about the administration of national parks needed to be aired in the discussion that surrounded the proposals for local government reform published in February this year. Although the commission considers that all national parks should ideally be run by an executive body with full planning powers and an appropriate staff (as is the case at present for the Peak Park and to a more limited extent the Lake District), agreement was eventually reached with the County Councils Association on a joint submission to the Department of the Environment.

The proposal is that each national park—except the Peak Park and the Lake District—should be administered by an executive committee of the local authority in whose catchment area the largest part of the park falls and that the committee should have both independent representatives and members from the other local authorities concerned. The two bodies also suggest that each park should be assigned a park administrator, 75 per cent of whose salary would be paid by central government.

The commission is also empowered by the 1968 Countryside Act to make grants to local authorities for the provision of country parks and picnic areas but the report has stern words for the seventeen of the fifty-eight administrative counties in England and Wales who have so far not submitted any suitable schemes.

The report clearly expresses the commission's concern at the preliminary explorations for minerals that are taking place in the Lake District and Snowdonia. At the public enquiry about an application by Rio Tinto Finance and Exploration Ltd to explore for gold and copper in Snowdonia, for example, the commission stated unequivocally that it was "entirely opposed . . . to all stages envisaged by the developers, for the reason that the developments to which they are intended to lead are wholly inconsistent with the purposes for which the national park was established".

Fig. 1 The Mawddach estuary and Cader Idris, Snowdonia, where exploratory drilling for minerals is taking place.

MARS

Continuing Progress

from our Soviet Correspondent

ALTHOUGH the current Soviet investigations of Mars have had a number of setbacks (notably the short effective life of the descent capsule) preliminary readings from telemetry data from the orbiting Mars-2 and Mars-3 stations have provided several interesting results.

The programme was originally designed as a three-prong attack—the descent capsule to transmit surface data and the two orbiting stations to take readings from essentially different orbits (Mars-2 from a highly elliptical 18 h orbit, with apocentre 25,000 km and pericentre 1,380 km and Mars-3 from an approximately 11 h orbit of pericentre 1,500 km) while the descent stage would provide readings of atmospheric temperature and pressure, wind velocity, chemical composition of the atmosphere and soil and also television pictures. Unfortunately, transmission from the surface, it is now revealed, ceased entirely after 20 s, so that it was impossible even to ascertain whether the experiments of the descent stage had begun to function satisfactorily; the telemetry from Mars-2, however, and the orbital section of Mars-3 are apparently providing satisfactory data.

The experiments aboard these craft include an infrared radiometer in the 8–40 μm range, to map the temperature distribution of the Martian surface; a device for studying the surface relief by measuring the amount of carbon dioxide along the line of sight, the amount of carbon dioxide being determined from the intensity of the 2.06 μm band by an infrared photometer; a device for measuring the reflective capacity of the surface and atmosphere in the visible range from 0.3 μm to 0.6 μm; a unit for measuring the radio brightness temperature of the surface in the 3–4 cm band, and of determining the dielectric permeability and temperature of the surface layer at a depth of 30–50 cm; a device for determining the density of the upper atmosphere and the content of oxygen, hydrogen and argon, using an ultraviolet photometer; two television cameras of different focal lengths, permitting both wide-range and high resolution photographs of the surface to be taken.

Initial telemetry readings have already provided a number of interesting results. The surface temperature, measured from the orbital pericentres by infrared radiometer, did not exceed −15° C. A point was observed on the night side of the planet where the temperature was some 20–25° C higher than the surrounding area. No explanation for this anomaly has so far been advanced.

Sharp differences in the brightness of the planet observed through different colour filters in the visible range have been noted, giving far fuller information about the colour differences of the regions of Mars than is obtainable from investigations from the Earth.

The water-vapour content of the atmosphere is, as expected, extremely low (at the points of observation it did not exceed 5 μm of precipitated water). Ultraviolet observations have shown the presence of monatomic hydrogen and oxygen in the upper layers of the atmosphere. As observations continue, it is hoped to obtain the variation of these components with height. Preliminary calculations indicate that monatomic oxygen is observed in the 400–1,000 km region and monatomic hydrogen at heights of 10,000–20,000 km.

Other observations have studied the intensity of thermal radiation in the radio range and the nature of its polarization along the planet's disk, enabling the effective temperature of the subsurface layer to be established and its dielectric permeability and mean density to be estimated.

A Better Deal in 1972?

THE scientists employed by the British Government must be hoping for a better deal in 1972 than they had in 1971. In spite of being awarded a pay increase in August that was backdated to January 1, 1971, they come out of the year with a reduced status compared with the Administration and Technology grades. Table 1 compares salaries within different grades of the Civil Service during 1971 with the salaries in 1969 and 1970.

The maximum salaries of the science class and the administration class were comparable until 1970 and similar to the top salary of the Senior Grade Engineer. The engineering grade, however, is currently having salaries reviewed and an increased pay offer is expected to be made early in 1972. If previous pay adjustments are any guide the salary of the Senior Grade Engineer will then be comparable to that of the Administrative Principal.

During 1971 the Institution of Professional Civil Servants (IPCS) fought a long battle with the Civil Service Department over new pay scales for the science category. The negotiations that started early in the year reached deadlock in June, went to arbitration in August and the tribunal's offer—a compromise between the IPCS's claim and that offered by the government—was at that time described by Mr William McCall, general secretary of the IPCS, as "deplorable".

In the two months between the breakdown of negotiations and the tribunal the dispute was highlighted by a series of public meetings that demonstrated the strength of feeling among the 17,000 scientists affected by the pay offer. Meetings all over Britain were well attended and the final gathering at the Central Hall, Westminster, attracted more than 4,000 disgruntled scientists and amply demonstrated the deep felt resentment about the government's pay offer.

One of the chief differences between the IPCS and the Civil Service during the negotiations was the emphasis to be placed on the findings of a pay research enquiry that made a study of scientists' salaries within and outside the Civil Service. The IPCS claimed that because the government employed so many of the scientists in Britain, industry tended to base its own salaries on salaries within the Scientific Civil Service. Therefore a pay comparison with outside organizations was meaningless. The IPCS favoured a greater emphasis on "internal relativities", so that in fact the close relationship between the salaries of the Administration, Technology and Science classes would be maintained. The Civil Service Department, on the other hand, stressed the pay research findings and it was no doubt well pleased with the report of the tribunal that included the statement "the award seeks to apply the principle of fair comparison and pay research that also takes into account the special features of a scientific career in the Civil Service".

There is no doubt that the disparity between the salaries of the science grades and the other grades that has manifested itself during 1971 will prove a severe obstacle to any plan for unified grading of the Civil Service beneath the undersecretary level. Unified grading was one of the recommendations of the Fulton report in 1968 and it has been the aim of the IPCS to institute this as soon as practicable. The Civil Service Department, however, is not enthusiastic about further merging of the categories although it has agreed in principle to the Fulton recommendations (see *Nature*, **233**, 365; 1971).

During the pay dispute Mr William McCall went on record as saying that scientists in the Civil Service would not be subjected to any further pay research enquiry. The IPCS has since worked towards achieving this end and it scored a success in persuading the Civil Service Department to agree to a joint committee to examine the criteria by which scientists' salaries should be determined in future. So far the committee has met twice and further meetings are planned for early in 1972. A Civil Service spokesman said last week that the meetings so far have been chiefly concerned with "gathering factual material . . . as a basis for further discussion".

Mr William McCall is hopeful that the present series of meetings will result in a decision on a basis for determining scientists' salaries that will not be dependent on pay research. He said last week that it was too early to say which way the wind was blowing but he was hoping that a suitable arrangement would be negotiated. A guide to the way the Civil Service Department will approach the joint committee is possibly obtained in the words of a spokesman for the department last October. He said, when discussing further mergers of the different grades within the Civil Service, that one of the difficulties of this would be that the Civil Service is committed to the practice of determining pay scales by comparison with outside organizations.

Another bone of contention that in this case is soon to be removed is the minimum age of promotion from a Senior Scientific Officer to a Principal Scientific Officer. Present policy is that 25 per cent of candidates be promoted between the ages of 30 and 34, which in fact has amounted to the minimum promotion age being 32. By contrast, the minimum age for an Administrative Principal is 27. Agreement has been reached recently to lower the minimum age for promotion to a Principal Scientific Officer, and as from January 1, 1972, the age limit will be between 28 and 32. This decision follows from the recommendations of the Fulton committee but the findings of the criticized pay research unit also showed that scientists outside the Civil Service achieved positions of responsibility at a younger age than scientists within the government. An engineer, however, has to be much older before he reaches the senior grade but this is also under discussion.

During the campaign for a better pay offer an appeal was made to the Prime Minister, Mr Edward Heath, to intervene on behalf of the scientists. This he refused to do, arguing that the IPCS's case did not "justify any improvements in the offers that have been made". In view of the offer that had been made to the Administration category at that time Mr Heath stressed that there was no attempt to discriminate against the scientist and that "continued progress in science and technology is essential to the future of this country and the government attaches great importance to the contribution made by the scientific staff within the Civil Service". The government scientist, now placed a poor third in the salary league table, has cause to reflect on Mr Heath's words. There is no immediate prospect of handouts.

Table 1 Maximum Salaries in the Science, Administration, and Technology Categories

Grade	1969	Jan. 1, 1970	Jan. 1, 1971
Principal Scientific Officer	£3,596	£3,902	£4,100
Administrative Principal	£3,596	£3,902	£4,400
Senior Grade Engineer	£3,625	£3,843	£4,208*

*Currently under review

NEW WORLD

Tenure under Fire

A STRANGE alliance of bedfellows has begun to mount an attack on one of the accepted and most jealously guarded facets of academic life—the institution of tenure. For long the acclaimed defender of academic freedom and of the right of university faculty members to pursue their teaching and research without fear of political interference, tenure is being criticized by radical students, conservatives and legislators of all kinds, although from widely differing standpoints. The upshot is that although it would be an exaggeration to describe the sum total of the criticisms as a frontal assault on the institution, those who support the concept of tenure are increasingly on the defensive.

Several factors have combined to cause discontent with the traditional concept of tenure—campus disturbances, financial stringencies in nearly all sectors of higher education and the continuing reappraisal of the whole role of higher education. Another increasingly evident factor is the growing unionization of university teaching staff and the consequent proliferation of collective bargaining in many institutions of higher education.

Many large universities and educational organizations have recently decided to take a close look at the way tenure is working and to see whether indeed it is as much a detriment as an asset to higher education. Last year, the President's Commission on Campus Unrest and the American Council on Education both concluded, although in a peculiarly indefinite way, that tenure is in part responsible for causing campus disturbances—chiefly through the influence on students of radical staff members who hold tenured positions and, among the universities that are conducting their own studies, Harvard has been the first off the mark with the publication earlier this month of a discussion memorandum which is, in many respects, a rousing defence of the concept and the workings of academic tenure (*Discussion Memorandum on Academic Tenure, prepared by the University Committee on Governance*).

The concept of tenure, which is essentially the right of an appointed faculty member to retain that position until he retires, is usually defended chiefly because it protects university staff from political harassment. Consequently, attacks on the system have tended in the past to come from conservative legislators who are entirely impotent to remove from office radical professors whose teaching may run counter to the accepted political order. A striking demonstration of the protection afforded by tenure is the case of Dr Clark Kerr, who was dismissed from the presidency of the University of Southern California, but immediately resumed his tenured position as professor of economics in the university. The board of regents, although able to dismiss him from the presidency, was powerless to remove him from his tenured position in the university.

Although the strident voices of those who accuse radical professors of hiding under the protective shield of tenure to ferment discontent on the campuses can still be heard, they have recently been forced to share their platform with the more radical critics of present university practices, who charge that the tenure system simply allows dead wood to remain in the universities by tying up tenured positions and allowing only limited scope for the infusion of new blood in the upper echelons of academe. A common rider to this criticism is that tenure has become an outdated instrument for protecting academic freedom since long-term contracts and the growing power of the unions on the campuses can be just as powerful a force against political interference in academic business.

Yet another criticism comes chiefly from educational administrators and legislators who argue that in times of severe financial stringency, inflexibility is imposed on the new staff appointments and on rearranging departments and faculties because tenured staff will soak up much of the available funds for salaries. There is also the argument that departments which have been built up to what later appears to be excessive proportions cannot easily be run down when they are filled with a multitude of staff in tenured positions. Such a situation, of course, offends the legislator's sense of business efficiency.

The Harvard memorandum deals with both these points by invoking the argument that turnover of staff is a sufficient guarantee that new blood will continually be called in to replace those older members of staff who leave the university, and, as for the suggestion that money could be saved by playing the market when hiring staff during times of financial stringency, the Committee on Governance tartly suggests "if the university were to take advantage of the present buyer's market and to do so without regard to quality, a considerable reduction in salary might well be gained". In short, the committee suggests that the guarantee of tenure at Harvard is often more important than mere salary and that without tenure it would probably require a larger salary carrot to entice quality staff members to the university.

Another commonly heard criticism of tenure is that it encourages faculty members to undertake more work outside the university, thereby decreasing institutional loyalties. The argument goes along the lines that since a faculty member is safe in the knowledge that his tenured position is in little danger of being taken away, he needs to devote less time to his university, and he can pile up more consultancy work for himself outside. The President's Commission on Campus Unrest was particularly insistent that faculty should be made to limit their outside commitments since a decrease in institutional loyalty is a major factor in spreading disillusionment with the established order in higher education. The Harvard committee gives short shrift to the notion that tenure is in some way responsible, however, suggesting on the contrary that it serves to insulate faculty members from economic pressures and that without the security of tenure faculty members may even be driven to seek outside sources of income.

But in the final analysis academic freedom is the chief factor in the argument about tenure. That is why many university members have been watching with interest the developments on the campus of Stanford University during the past few months. A radical faculty member at Stanford was suspended from teaching and brought before a committee of eminent professors charged with the task of advising whether he should be dismissed. The faculty member, Dr H. Bruce Franklin, was suspended chiefly because of his participation in a demonstration which led to the shouting down of Mr Henry Cabot Lodge, the former US ambassador to South Vietnam, when he gave a lecture at Stanford in January, and also because he is alleged to have incited students to occupy the university computer centre a month later—a demonstration which led to several arrests and injuries. Dr Franklin was suspended in February by Mr Richard Lyman, the university president, who asserted that his activities constituted a threat to the workings of the university. The committee report was sent to Mr Lyman a week before Christmas but no final decision on whether Dr Franklin would be dismissed had been taken when *Nature* went to press.

BEHAVIOURAL RESEARCH

The End of Congress

by our Washington Correspondent

A NEW threat to the American system of government has come from a respected member of the scientific community and, if at least one congressman is to be believed, the threat should be taken very seriously. "I rise today in the closing hours of the first session of the 92nd Congress to discuss events and trends which may well eventually see the permanent closing of the Congress itself," Cornelius E. Gallagher said last week in a speech reported in the *Congressional Record*. The object of Mr Gallagher's political hyperbole and dread fears is Dr B. F. Skinner, whose book *Beyond Freedom and Dignity* has been riding high in the best selling lists recently. Mr Gallagher is worried not so much that Dr Skinner's ideas "denigrate the American traditions of individualism, human dignity and self reliance", but that he was given federal money with which to advance them.

"I wish to disclose to my colleagues this afternoon," Mr Gallagher tells shocked readers of the *Record*, "that the National Institutes of Mental Health has granted to Dr B. F. Skinner the sum of $283,000 for the purpose of writing *Beyond Freedom and Dignity*." Mr Gallagher hastily tries to assure his readers that he does not want to see scientists muzzled in case they produce results and ideas that run counter to the accepted way of life, since he points out that Dr Skinner has every right as an American citizen to free speech, but he is concerned that the federal government may be sowing the seeds of its own demise by subsidizing the advancement of Dr Skinner's ideas.

According to the General Accounting Office, Dr Skinner's grant was awarded by NIMH for a ten year period to free him from teaching and research responsibilities (Dr Skinner is chairman of the psychology department at Harvard) so that he can pursue "scholarly activities". The result, according to Mr Gallagher, who describes himself as not a literary scholar, nor a trained psychologist, is a book which seeks "to alter modern life by conditioning the behaviour of each citizen by positive or negative reinforcements".

What can Congress do to prevent agencies such as NIMH doling out federal money to scientists who have the audacity to use it to criticize the system of government and the American way of life? The answer, according to Mr Gallagher, is not to cut off such funds, but to provide Congress with a means of combating "antidemocratic thoughts launched with federal funds . . . to assure that the twilight of the twentieth century does not see the total eclipse of the legislative branch". It so happens that Mr Gallagher has proposed the setting up of a Select Committee on Privacy, Human Values and Democratic Institutions that may do the job. Perhaps a better name for the committee would be the select committee on un-American activities.

RESEARCH FUNDING

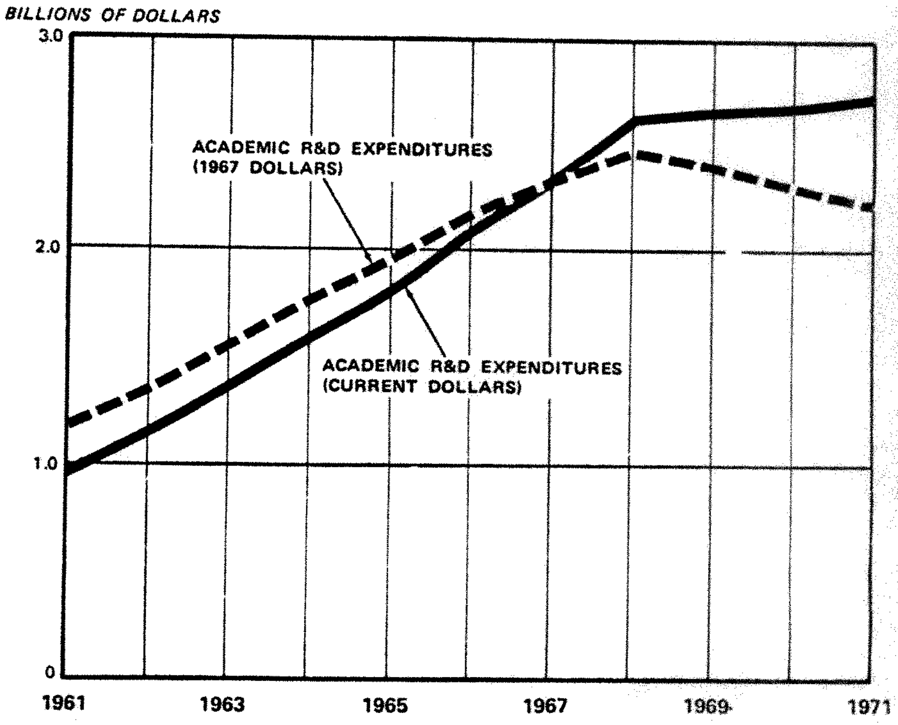
On the Downgrade

by our Washington Correspondent

Two reports released by the National Science Foundation bear witness to the recent decline in federal funding of research and development. The first report, published last month, shows that inflation has doubled the costs of academic research during the past ten years, and the other shows that spending on industrial research and development, in constant dollar terms, dropped eight per cent between 1969 and 1970. The net effect is that what seems to be a yearly increase in funds for academic research for every year between 1961 and 1971 turns out to be a decrease in purchasing power between 1968 and 1971 (see graph), and as far as industry is concerned, six per cent fewer scientists and engineers were employed on research and development in 1970 than a year previously.

One of the more surprising and significant aspects of the report on academic research funding is the finding that inflation has pushed up the costs of academic research faster than it has pushed up general prices. In the early years of the 1960s, for example, the costs of research rose at almost double the rate of general prices, and the upshot is that $1 million in 1961 would have shrunk in purchasing power to $670,000 in 1971. Also, between 1968 and 1971, in constant dollar terms, funding dropped by 3.4 per cent a year. One implication of this finding is that if expenditure on research and development is calculated simply in terms of general price inflation, the actual level of funding in terms of purchasing power will be exaggerated.

As for the performance of research and development by industry, the NSF figures show that the total spent in 1970 amounted to $17,900 million—three per cent less than the previous year, or eight per cent less in constant dollars. The entire drop in industrial research and development spending, the report points out, can be accounted for by a decrease in federal funds to industry. Between the two years, the federal share of industrial research and development funding dropped from $8,400 million to $7,900 million—the lowest level since 1965. Basic research performed by industry dropped from $620 million in 1969 to $599 million in 1970, applied research remained constant at $3,300 million while development fell from $14,400 million to $14,000 million.



Comparison of academic research and development expenditures in current dollars with deflated dollars for the financial years 1961–71. Taken from *Current Dollars—National Patterns of R&D Resources. Funds and Manpower in the United States, 1953–71* (NSF 70-46).

Strength to the Research Councils' Arms

This article, commenting on the Rothschild and Dainton reports, is by Mr William McCall, general secretary of the Institution of Professional Civil Servants.

MY first comment about the present debate on civil science—the government's contribution to it and how it should be managed—is that I hope that it will be the last for some considerable time. For the past decade there has been a virtually non-stop succession of reviews, with hardly a break in the ferment of uncertainty and change. Some but recently established research councils have already been under threat of extinction, and there has been growing criticism of expenditure which cannot be seen to "pay off" quickly and directly. Inevitably, morale has suffered and we urgently need a period of stability.

It is important therefore to ensure that the right decisions are now taken. At the end, not everyone will be satisfied, but there should be no needless controversy about the way in which the decisions are taken. It is essential that all points of view should be carefully assessed. More time for consultation should be given and at this stage an extra month would make a great difference.

My second point is a plea that the dangers of over-simplification should be avoided. In the early stages of the debate the issues have been posed, inevitably perhaps, in terms of Rothschild versus Dainton. The use of colourful language has stimulated the argument but there is a danger that it will not illuminate the issues. Although there is a good deal to be said for the notions underlying it, a customer/contractor relationship is also a dangerous over-simplification. If the issues become posed and polarized in this way the outcome will almost certainly be unsatisfactory. It is a great pity that a joint review was not undertaken by Rothschild and Dainton.

This is not such a fanciful idea as it might appear at first sight. There is, for example, much in the Dainton report with which no informed observer could disagree. Thus, in paragraph 27, Dainton states:

"the pervasiveness of the consequences of science, the diversity of its users, the complexity of the connexions between basic research and related economic benefits, the close relationships between different scientific disciplines, and the unifying importance of training in the methods of research, are, we believe, the most important general points about the nature of the scientific activity that we have to bear in mind in considering the Research Councils".

Later, in paragraphs 30, 31 and 32, the pressure on government resources, the sophistication factor, and the growth of big science are correctly diagnosed as factors which point to increasingly international collaboration, to a need for selectivity in the support of science, and to the need for research councils to become increasingly well-informed about national needs and objectives. And, as Dainton states in paragraph 32,

> "increasingly we need to know more about ways in which such new knowledge can be used in harmony with economic and human needs of the situation and this calls for a much closer integration between the natural sciences and the social sciences . . .".

Similarly, we should all be grateful to Lord Rothschild for the way in which he debunks a number of familiar questions about research and development and scientific policy. His idea of a general research surcharge is a valuable one although it will be necessary to make a careful assessment as to whether the figure he suggests is right. His emphasis on the importance of multi-functional laboratories should also meet with general agreement. His various recommendations on staffing policies support and strengthen the recommendations of the Fulton Committee and are appropriate and timely. In particular, he is certainly right about the need to strengthen the scientific competence of many Departments of State.

It is, however, also important not to minimize or to disguise the difference in the approach of these reports. Rothschild appears to shift responsibility for determining what research should be done to the customer which, in the case of the research councils, will be mainly the appropriate government department. Certainly the "customers" should not be excluded. They do need to be closely involved, but the emphasis should be on involvement and participation. The research councils must and will continue to play the major role in basic science. The working scientist must also participate, and the arrangements should provide for a dialogue at all levels. And disagreements should be brought into the open through annual reports of research councils and of the other government research establishlishments so that decisions are not taken behind the closed doors of government but in a way in which Parliament and the public can exercise some influence.

The argument about organization cloaks the more important argument which is about resources. The issues really relate to the scale of these resources, to priorities, to accountability, and to exploitation. The objective in the exercise should be to maximize resources, accountability and exploitation and to determine priorities acceptable to scientists, Parliament and public.

From the comments which have already been published in various journals and newspapers, it is evident that there is no shortage of prophets of doom. But I do not take such a pessimistic view of the possible outcome of the consultations which are now taking place. It would help if the government would make clear that there is to be no blind cutting back in resources. The future organization must give emphasis to the freedom of the scientist in basic research as well as identify priorities. Scientists, on the other hand, must not jib at arrangements which provide for greater accountability at the same time as it is right to insist that they participate in the decisions which so directly affect them. The government must accept that the research councils and the other public research and development establishments should be fully involved in the decisions on priorities and in maximizing the returns on the investment which the country makes in science, research and development.

NEWS AND VIEWS

Nonvelocity Redshifts in Galaxies?

WHAT could be more confusing for astronomers than nonvelocity redshifts in quasars? It now seems that there may be nonvelocity redshifts in normal galaxies. The first claim that quasar redshifts were not caused by Doppler velocities of recession (H. Arp, *Science*, **151**, 1214; 1966) was met with general disbelief. Some theoreticians considered models for gravitational redshifting mechanisms, but these models foundered on the difficulties of large masses and sharp gravitational gradients in the strong gravitational fields which would smear out the observed spectral features in the quasars. So the disbelief in nonvelocity redshifts deepened.

In spite of this inhospitable theoretical climate, some observational claims were made that there was increasing evidence that quasars were closer than their redshift distances. As if the whole matter were not bad enough, some evidence, advanced from the very beginning, had not only quasars but some radio galaxies and compact galaxies also showing spuriously high redshifts. Finally, evidence was put forward that some fairly normal companion galaxies had excess redshifts (H. Arp, *Nature*, **225**, 1033; 1970). Almost nobody took this new heresy seriously enough to even debate it and only the mildest of controversy ensued (B. M. Lewis, *Nature Physical Science*, **230**, 13; 1971; and H. Arp, **231**, 103; 1971).

The embarrassing subject did not, however, go away; early work on the Virgo cluster of galaxies by E. Holmberg had indicated increasing redshifts with fainter galaxies at the same distance, and additional independent measures by W. Tifft at the University of Arizona were interpreted by him as showing nonvelocity redshifts for many of Virgo cluster members. Later Tifft concluded that many Coma cluster galaxies also showed excess redshift. The Finnish astronomer, T. Jaakkola, has now independently reviewed the redshift data for groups and clusters of galaxies, and on page 534 of this issue of *Nature* he concludes that the spirals, and particularly the Sc spirals, show systematically higher redshifts than ellipticals and S0 galaxies at the same distance.

The importance of Jaakkola's results and the really staggering difficulty involved is that the anomalously redshifted spectra refer to galaxies composed of stars and gas presumably of the same kind as the lower redshifted galaxies. What could be different about a star in an Sc galaxy compared with one in an E galaxy that would give the former an intrinsic relative redshift?

If the observations are correct, and if the interpretation of nonvelocity redshift is correct, there are only two possibilities. First, that conventional physics by some presently unknown and complex model of particle or plasma scattering can give some galaxies excess redshifts relative to others; or, second, that physics at some times and places (one galaxy) is different from physics at another time and place (the other galaxy). There was, perhaps, a small movement starting in this last direction (H. Arp, *Nature*, **223**, 386; 1969), but then Hoyle and Narlikar (*Nature*, **233**, 41; 1971) entered the theoretical arena. They accepted the anomalous galaxy redshifts and investigated a physics where mass was conformally invariant, producing a theory which they claim will pass all the conventional observational tests of relativity. It allows a gravitational constant which is a function of time—as in early theories considered by Dirac and Jordan.

Although it has not been specifically formulated in the Hoyle and Narlikar theory, the possibility has been opened that the mass particles which constitute the atoms in the stars that make up different galaxies could couple to the mass field of the universe differently as a function of time and place. The atoms made up of the smaller mass particles would then radiate their characteristic lines at longer wavelengths. This theory could furnish a start in understanding the Jaakkola results and all the anomalous results which led up to them. On the other hand, the acceptance of anomalous redshifts for certain kinds of galaxies on the strength of the observational evidence alone would furnish a powerful reason for accepting the new mass coupling theories.

The sweeping and fundamental changes involved in accepting this more Machian view of the universe and physics are so drastic that astronomers will no doubt proceed very sceptically and slowly; but an increasing number of workers are becoming impressed with the observations. The most recent evidence on quasars gives additional support to nonvelocity redshifts. In one case, the long base line radio observations on the quasar 3C 279 show its parts to be separating at ten times the velocity of light if it is at its redshift distance. Only very special models could prevent its having to be much closer than its redshift distance in order to preserve the velocity of light as a physical limit. In another case, H. Arp has shown the quasar Markarian 205 to be connected by an actual luminous filament to the much lower redshift spiral galaxy NGC 4319 (*Astrophys. Lett.*, **9**, 1; 1971). It has been argued that there is continuity of physical parameters between quasars and other kinds of galaxies. If nonvelocity redshifts must be accepted for quasars, then their acceptance for more normal galaxies may be a step more possible.

If these observational inductions are accurate, astronomers may be at a basic turning point in understanding of physical laws. This has vast implications and, if that is the case, the next few years are likely to be very exciting for both observational and theoretical astronomy.

TERATOGENESIS

Preventing Birth Defects

from a Correspondent

THE first annual prize of L'Institut de la Vie was awarded to Dr William G. McBride of the Sydney Lying-in Hospital by an extremely distinguished panel of jurors. Dr McBride discovered the teratogenic effects of thalidomide. He refused to accept the prize money for himself and instead raised an appeal in Australia to increase the amount (250,000NF) by a factor of 25. He is half-way to his target, so that it was fitting that L'Institut de la Vie held a meeting in Paris on December 2–4 to discuss strategy in preventing birth defects when possible and in alleviating their physical, psychological and social effects.

The problem has at least three major aspects. First, it is plain that for many countries there are no reliable statistics of the frequency of even the commoner foetal and neo-natal defects. Dr McBride gave a lucid, but sobering, account of the obviously thorough and efficient screening of mothers, foetuses and neo-nates at his hospital. In New South Wales roughly 5 per cent of all children are seriously defective: 1.5 per cent have a major physical defect such as spina bifida, 1 per cent suffer from severe cerebral palsy and 2.5 per cent from mental retardation severe enough to prevent their taking an effective place in society. These figures are from an advanced, well nourished and healthy people, but even so the irreducible minimum of birth defects is clearly far from achievement.

Brillat-Savarin (*Physiologie du Goût*, 1825) said: "La destinée des nations dépend de la manière dont elles se nourrissent". His words were dramatically reinforced by Dr R. G. Whitehead (Kampala) who described the effects of protein malnutrition in a relatively undeveloped country. Protein malnutrition leads to a continuum of syndromes, from kwashiorkor, a disease caused principally by an excessive ratio of carbohydrate to protein in the diet, to marasmus, caused by plain starvation. The result of malnutrition in these forms is an increased susceptibility to disease and a prevalence of metabolic disorders associated with a reduced amino-acid pool. Although many of the effects on young children are reversible, permanent damage can be caused to the central nervous system, particularly if a foetus or young child is malnourished during one of several critical periods during development. It seems typical, in underdeveloped countries, that the problems posed by malnutrition are so severe that the occurrence of birth defects with more subtle causes is relatively insignificant. In any case, the relevant statistics are almost non-existent.

The second aspect of the problem is the recognition of new teratogens, which can often only be done by epidemiological methods. Professor J. R. Miller (University of British Columbia) emphasized that it is essential to have fast, accurate and comprehensive recording of the occurrence of birth defects so that novel or unusual patterns can be quickly recognized. Clearly, the data storage and analysis must be carried out by a centralized computer system in each country. There are many pitfalls, however. For example, an outbreak of phimosis was traced to a single paediatrician who used the diagnosis to justify the circumcision of all male babies. More important is the fact that a very small incidence of some abnormality may have to be recognized very quickly if a tragedy of major proportion is to be avoided. It still seems that an experienced clinician is most likely to do this: Dr McBride suspected thalidomide after seeing six "thalidomide babies".

Third, once these problems are solved, come the questions of prevention and cure. One of the most successful cases is the identification of rubella as a teratogenic disease with the prospect of its impending eradication in developed countries. In a more dramatic vein, the technique of amniocentesis in which amniotic fluid containing foetal cells is removed from the mother offers many potential benefits in cases where there is a high probability of a genetic or chromosomal abnormality. As Dr K. Hirschhorn (New York University School of Medicine) said, it should now be possible, in theory at least, to eradicate Down's syndrome (mongolism) by recognizing its karyotype in foetal cells, and aborting the foetuses concerned. Even so, some mothers still refuse abortion. Foetal cells removed by amniocentesis can also be cultured and assayed for enzymatic deficiencies in cases where inborn errors of metabolism are suspected. Again, some degree of indirect genetic engineering by therapeutic abortion is possible, and the impression is that progress in this sphere is extremely rapid. It should become possible to obtain samples of foetal blood to determine blood group and it might also be possible to induce the synthesis of enzymes not already present.

The impression left by the meeting is that clinical medicine is advancing rapidly in combating teratogenesis, but that there are still no useful contributions from the more theoretical biologists who were well represented. Fundamental research is obviously essential, but the gap between basic science and clinical science seemed unusually wide. One point, which was rather unemphasized, was that the biggest single contribution to the removal of birth defects would be the reduction of malnutrition, which can only be done by population control.

What Colour is the Sky on Venus?

THE National Aeronautics and Space Administration is not yet anticipating sending astronauts to Venus, let alone a poet or a painter. But in spite of the distance of at least 4×10^7 km that separates the Earth from one of its nearest planetary neighbours, some quite detailed information and reasonably based speculation about the nature of the Venusian atmosphere are now forthcoming.

A further contribution to the discussion will be published in next Monday's *Nature Physical Science* (January 3) in which A. C. Aikin of the NASA/Goddard Space Flight Center discusses ion clusters and the Venus ultraviolet haze layer. In his article he cites observations of electron concentrations in the Venusian atmosphere as a function of height and discusses the possible composition of the complementary positive ion concentration.

If, as is thought, CO_2^+ is the principal ion, then Aikin argues for the importance of clustering of this ion by the addition of CO_2 or of almost any other molecule which may be present. He suggests that these condensation nuclei eventually build up to micron-sized particles by coagulation of clusters. The object of such detailed speculation is to offer an explanation for the observed ultraviolet haze layer on Venus, if not also the yellow cloud layer at lower altitudes. The compositions proposed would suggest an atmosphere much more inhospitable than anything yet produced on Earth.

Aikin stresses the likely importance in all this of the reactions of electrically charged particles. The advantage that these have over neutral species is the long range of their interactions so that high rates of reaction, even at low number density, are produced. (The rapidity of such "condensation" effects was, of course, put to good use by Wilson when he invented his cloud chamber.) Similar effects certainly play a part in the behaviour of the Earth's atmosphere, especially during thunderstorms. Although the composition of the Venusian atmosphere may be very different from that of the Earth's, initial arguments must be based on the supposition that some features of both are similar. Only further investigation by space probes can show whether arguments based on such similarities can be sustained.

PROTEINS

Albumin, Age and Anion

from our Molecular Biology Correspondent

BOVINE serum albumin is above all a protein chemist's protein; and if its mesmeric effect within such circles does not always communicate itself to those outside, some new studies on aspects of its behaviour deserve to be advertised more widely, both as immaculate pieces of research and for their wider biochemical implications.

Foster and his associates have for many years now been studying the microheterogeneity of bovine serum albumin, which is manifested in some of its physical properties, and they have attributed it to the co-existence of states differing in some degree in their disulphide pairings. Nikkel and Foster (*Biochemistry*, **10**, 4479; 1971) have now shown that in bovine mercaptalbumin (a component of the protein containing a solitary unpaired thiol, in addition to the many disulphide bands), an equilibrium mixture of two states is spontaneously generated on standing in solution, in a process catalysed by the thiol group. When a solution is aged in this way, free boundary electrophoresis profiles show the progressive formation of a second component (not incidentally detectable by polyacrylamide gels). The reaction is dependent on *p*H, in accordance with the view that disulphide exchange proceeds by way of the ionized form of the thiol group. When the free thiol is blocked by carboxymethylation, the reaction is completely inhibited. The ageing process is reversible: starting with either component an equilibrium position is established with time, in which the two concentrations are about equal.

The inference from all this is that the reaction is indeed a thiol-catalysed disulphide-exchange equilibrium. This interpretation is supported by the restoration of the equilibrium in the carboxymethylated albumin, when an extraneous thiol, mercaptoethanol, is added. That the catalyst is the reagent itself, rather than new thiols introduced into the albumin by reduction, is shown by the failure of the protein to incorporate added labelled carboxymethyl groups when exposed to the alkylating agent following ageing.

The question now remains whether the thiol group of mercaptalbumin is itself a partner in an exchange reaction, such that the free thiol in the species formed on ageing belongs to a different cysteine in the chain. Nikkel and Foster have answered this by carboxymethylating the separated components, fragmenting them with cyanogen bromide, and showing that in both cases the label on the reagent was in the N-terminal fragment of the albumin. A tryptic digest of this fragment was in each case subjected to peptide mapping, and the label was found again to reside in the same spots in both cases. The original thiol is thus regenerated after participating in a relay disulphide exchange process. At least four half-cysteine residues must be implicated in the exchange, and must be sterically related in such a way that the conformational distortion on passing from one form to the other can be readily absorbed. By contrast then to the familiar situation in the many proteins with only a few disulphide bonds that have been shown to reform uniquely from the reduced state in regenerating the native conformation, there are here two stable conformational states of essentially equal energy.

It is known that the transition between the native and the aged forms is inhibited by the presence of the fatty acid anions, which are strongly bound to the albumin as it is normally isolated. Lovrien and Sturtevant (*ibid.*, 3811) have measured the enthalpy of binding anions including dodecyl sulphate, to bovine serum albumin by calorimetry. For both iodide and dodecyl sulphate, there is one very strong binding site, as well as several weaker sites. When combined with free energy data, the enthalpy for the strong binding process turns out to correspond to a prodigious negative entropy of binding. It is impossible to account for this effect in terms of changes in ionic solvation, and it must therefore be supposed to be conformational in origin. The attachment of the ion thus seems to eliminate conformational freedom present in the native structure.

New light on the extraordinary ability of albumin to function as a kind of sponge for all manner of ionic and non-ionic ligands comes also from Jonas and Weber (*ibid.*, 4492). They have prepared a chymotryptic digest of the protein, and find that a large proportion of the residues known to be present in binding sites, namely the hydrophobic amino-acids in general, tryptophan and also arginine, are present in high concentration in the collection of small peptides that are formed. Using the binding of the fluorescent ligand, anilinonaphthalene sulphonate, as a criterion, they find that the sites are not active in the peptide mixture, neither will the high-molecular weight residuum bind the ligand significantly. When, however, the small peptides are chemically coupled to the essentially inert protein, lysozyme, they acquire again the ability to bind the ligand almost as strongly as the native albumin. Neither the free lysozyme nor the high-molecular weight fraction of albumin coupled to lysozyme possess appreciable binding capacity. It seems therefore that quite small tracts of sequence carry the ligand-binding proclivity, but in order to function they evidently require the degree of immobilization, or the dielectric milieu, provided by a macromolecular matrix.

A Candidate Human RNA Tumour Virus

IN next Wednesday's *Nature New Biology* (January 5) McAllister and seven colleagues including Huebner describe some of the properties of an intriguing C-type RNA virus which is liberated by human sarcoma cells (RD 114 cells) that have been passaged in kittens. Although it is premature to state that this virus is, beyond doubt, of human rather than feline origin, few people will quarrel with McAllister *et al.* when they say that "this virus still appears to be the most likely candidate for a human C-type virus yet described".

The original RD human rhabdomyosarcoma cells were screened as long ago as 1969 by McAllister *et al.* who found no evidence that they produce C-type RNA viruses. Last year, however, McAllister *et al.* inoculated some of these human cells into kittens where they gave rise to disseminated tumours, the cells of which retained the human chromosome complement. Subsequently some of the cells of these tumours, and a line (RD 114) of cultivated cells selected from tumour material, were found to be producing C-type RNA virus particles. In short, passage of these human cells in kittens had resulted in their starting to produce an RNA virus; this, of course, raised two possibilities: either the virus-free cells had been productively infected by an endogenous cat RNA C-type virus or the human cells had been triggered to support the replication of a previously latent, human C-type virus.

What McAllister *et al.* now report is the progress they have made towards deciding between these alternatives. Neither sonicates of the RD 114 cells nor preparations of disrupted RD 114 virus particles cross-react in complement fixation tests with antisera directed against the group (species) specific gs1 antigens of feline, murine, rat, hamster or avian leukaemia viruses. Both the RD 114 cells and the virus they produce do, however, carry the interspecies specific gs3 antigen which is common to all the mammalian C-type RNA tumour viruses. Furthermore, the RD 114 virus particles have all the biochemical and biophysical properties of a typical C-type RNA virus. In other words, McAllister *et al.* have a C-type virus produced by human cells which is antigenically distinct from all the recognized groups of C-type viruses.

LABYRINTHODONTS

Amphibians of the Coal

from our Vertebrate Palaeontology Correspondent

THE large and varied amphibians known as labyrinthodonts were the first colonists of the land. They include some six or seven groups which differ principally in their vertebral structure. One group, characterized by having two disk-like centra in each vertebra, is commonly known as the Embolomeri. In a comprehensive and well illustrated review of this group (*Encyclopedia of Paleoherpetology*, Part 5A; Stuttgart, Fischer) A. L. Panchen has preferred to revive the original name Anthracosauria—a term which refers to the coal deposits in which most members have been found.

The long snout, the elongate body with (at least in the best known form, *Archeria*) a long tail bearing a dorsal fin and the relatively small limbs, all suggest that these amphibians were aquatic predators which swam by lateral undulations of both the body and tail, aided by paddling with the hind limbs, which may have been webbed. Such a mode of life is supported by their preservation in coal deposits. Panchen points out that they are never found in humic coals, but usually in sapropelic coals, laid down in the deep anaerobic mud which formed in stagnant conditions. The varied fish fauna of these coals includes xenacanth sharks; Panchen notes that these are unlikely to have had methods of aerial respiration, and infers that the environment was a large lake, with oxygenated surface waters but stagnant depths, and with no seasonal overturn of the water.

Anthracosaurs are known from the United States, Great Britain and Bohemia—all, in pre-drift times, in western Laurasia—and Panchen shows that all the localities were close to their contemporary equator. The earliest (Lower Carboniferous) forms all came from the eastern United States or Great Britain; since the earliest known amphibians, the ichthyostegids, were found in Greenland (in those days, adjacent to Western Europe), Panchen speculates that this may in fact have been the area in which tetrapods evolved.

The generally accepted theory of relationship between the labyrinthodont amphibian groups is that of Romer, who believes that the double disk condition of the vertebrae of anthracosaurs evolved from a condition similar to that known as rhachitomous, in which neither part of the centrum forms a complete disk. This view implied that early anthracosaurs would have had rhachitomous vertebrae, and this prediction seemed to be substantiated by *Pholidogaster*. This early Mississippian (Lower Carboniferous) labyrinthodont from Scotland was based on a skeleton which proved to have rhachitomous vertebrae. Though the skull of this specimen was obscured by a hard ironstone matrix, another skull (the horizon and locality of which were unknown) had earlier been attributed to *Pholidogaster*, and was of anthracosaur pattern. Panchen, however, is convinced that the two specimens are not related, that their matrices are different, indicating that they did not come from the same horizon, and that the ornament on the skull of the original specimen of *Pholidogaster* (which has now been partially cleaned) is unlike that of any anthracosaur. He suggests that the more solid type of vertebral centrum, found both in the anthracosaurs and in their relatives the seymouriamorphs, was the original condition for these two groups. He believes that it evolved primarily as an adaptation for terrestrial locomotion and only later proved also adaptable to the environment and locomotion of the elongate anthracosaurs.

Panchen's suggestion seems to be supported by *Mauchchunkia*, an early Mississippian anthracosaur from Greer, West Virginia, described by Hotton (*Kirtlandia*, No. 12, 1 ; 1970) in which the body is short and the limbs are stout. Two other amphibians from Greer have been described by Romer (*Kirtlandia*, Nos. 6, 1969; and 10, 1970); one is an anthracosaur, the other is an ancestor to a peculiar group of Upper Carboniferous labyrinthodonts known as colosteids. It is clear that this fauna is likely to reveal new and unexpected aspects of very early amphibian evolution, and further descriptions will be eagerly awaited.

BIOTELEMETRY

Tracking of Wildlife

from a South African Correspondent

WIDESPREAD interest in biotelemetry has existed in South Africa only for the past five years or so. The good attendance at the symposium on biotelemetry, arranged by the Council for Scientific and Industrial Research (CSIR) at the University of Pretoria (November 29–December 2), suggests, however, that this field is now firmly established.

In a keynote address on sensing and transmitting biological information from animals and man, Professor R. Stuart Mackay (University of Boston) delighted the biologists by making it all sound terribly easy. The other extreme was represented by Professor John R. Tester (University of Minnesota), who described the complex tracking system used by him, which involves continuous tracking of up to fifty-two animals at a time by two continually rotating antennae. Signals are fed into a

Pokeweed Mitogen and Immunoglobulin Synthesis

POKEWEED mitogen is one of the plant lectins which, like the better known phytohaemagglutinin (PHA), can be used to stimulate lymphocytes *in vitro*. In the early days of work of this kind, particularly in relation to PHA, there was much argument as to whether the lymphocyte stimulation led to antibody production and was thus equivalent to an immune response. As so often in cellular immunology there were two contrasting opinions and the dialogue was fierce. Now the waters are calmer, at least with PHA, and there is general agreement that activation of lymphocytes with this material leads to protein synthesis but not to large scale production of immunoglobulins. In next Wednesday's *Nature New Biology* (January 5), Parkhouse, Janossy and Greaves claim that activation of B with pokeweed mitogen leads to the production of immunoglobulins.

Parkhouse *et al.* incubated lymphocytes from either normal mice or from animals with a quantitative deficiency of T cells with pokeweed mitogen or with PHA. After four days the cultures were incubated with radioactive leucine and the cultures were then harvested. The supernatants and cell pellets were treated separately in such a manner as to quantitate any radioactive immunoglobulins produced. It was found that cells stimulated with pokeweed mitogen had a greater percentage of protein synthesis devoted to the production of immunoglobulins than did the PHA-stimulated cells. This selective stimulation of immunoglobulin synthesis also seemed to be more marked in the cells from T-cell deficient mice than in cells from normal animals. In other words, the effect of pokeweed mitogen in inducing immunoglobulin synthesis is likely to be on B cells rather than T cells. The immunoglobulins which were synthesized were almost entirely IgM and free light chains; no significant amounts of IgG were detected.

What kinds of IgM are synthesized by the B cells in, for example, a myeloma? It is not thought that the IgM produced is an anti-pokeweed mitogen antibody though no tests of this unlikely possibility seem to have been made. Parkhouse *et al.* prefer to think that the response they describe is essentially "aspecific" and that the immunoglobulins secreted will prove to be heterogeneous, or polyclonal in the accepted jargon. If they are wrong the clonal selection hypothesis will take a heavy jolt.

receiving and recording system, with fifty-two channels, and data are continuously recorded on 16 mm film, punched on computer cards and then fed to a computer which prints out any desired information about the animal and its movements.

Perhaps equally complex is the system described by Dr J. J. Craighead (Montana Cooperative Wildlife Research Unit) to record environmental and physiological data from the winter den of a hibernating black bear. The system was made available by NASA, and involved an IRLS unmanned data station with twenty-eight channels. In what he called a feasibility experiment Dr Craighead and his colleagues monitored temperature and light intensity with sensors placed at various points in and around the bear's den. Signals from these sensors were interrogated at 12-hour intervals by the IRLS platform and were transmitted to Fairbanks tracking station. From Fairbanks, data were sent by telephone line and microwave link to the Nimbus data processing centre at NASA's Goddard Space Flight Center near Washington DC, where the data were processed, printed out by computer and sent to the experimenter. The system used was probably far more complex than was needed in this particular case but, as Dr Craighead pointed out, it would have advantages in work on animals in remote areas.

Some of the local work reported involved straightforward radio tracking of medium-sized and large mammals; for example, studies have been made by Dr P. P. de Moor and Dr F. E. Steffens (CSIR) on vervet monkeys, by Mr P. M. Hitchins (Natal Parks Board) on black rhino, by Mr N. Owen-Smith (Natal Parks Board) on white rhino, and by Dr D. H. M. Cumming (National Parks, Rhodesia) on warthog. There were also some reports on physiological monitoring, for example Dr E. D. Smith (CSIR) on activity and heart action in sharks, Dr G. D. Brown (CSIRO, Australia) on temperature, respiration rate and activity in sheep and kangaroos, and Dr A. M. Hart-hoorn (Transvaal Nature Conservation) on temperature in various wild ungulates.

A discussion panel under Professor J. Meester (University of Pretoria) came up with two recommendations emphasizing the important part that the CSIR has played, and is expected to play, in biotelemetry: that a committee be set up, under the aegis of the CSIR, to coordinate future developments in bioengineering; and that a central workshop be set up within the CSIR, where further research and development can be undertaken, and which can lease equipment to research workers for specific projects.

COMMUNICATION

Chimp Language

from our Animal Behaviour Correspondent

APPARENT differences between animal communication and human language continue to dwindle as more and more is discovered of the capabilities of animals. It has often been maintained that one of the distinctive features of human language is its creativity, humans, unlike other animals, possessing the ability to invent new signals or to put existing ones into new sequences. But the remarkable success of R. A. and B. T. Gardner in teaching sign language to a young chimpanzee named Washoe showed that this distinction is not always valid, because Washoe showed definite evidence of creativity in just this sense. (A preliminary account of the Gardners' work is to be found in *Science*, **165**, 664 ; 1969, but Washoe has progressed considerably since then.)

Another distinguishing feature was thought to lie in what animals communicated, the idea being that animals conveyed no more than their current mood or motivation and could not transmit information about their external environment. Studies on a number of different animals have shown that this is not the case and E. W. Menzel (*Folia Primat*, **15**, 220; 1971) has recently provided more evidence that animals can communicate about their environment.

Menzel experimented with a group of eight young chimpanzees which were all well known to one another. Out of sight of the rest of the group, one of them, called the leader, was shown the whereabouts of a hidden pile of food but was not allowed to eat it. The leader was then reunited with its companions and the whole group was released together into the test area. As the leader headed for the food, the others followed or even ran ahead of their leader.

If the leader had been shown not food but a plastic toy or other fear-inducing stimulus, the behaviour of the others was quite different (more cautious) even before the toy was visible to them and even if the toy had been removed in the meantime. In trials where there were two leaders and one had been shown fruit (a highly preferred food) and the other had been shown vegetables (less preferred) the whole group tended to go straight to the fruit, implying that there had been some sort of "pooling of information").

It is interesting that in most cases there was little obvious signalling between the animals, that is, no conspicuous calls or gestures. Communication between these chimpanzees was thus accomplished through some very subtle aspect of their behaviour.

Mechanism of Kasugamycin Resistance

LAST September in *Nature New Biology* (**233**, 12; 1971) Helser, Davies and Dahlberg reported the striking discovery that the resistance of *Escherichia coli* to the antibiotic kasugamycin stems from a change in the 16S RNA moiety of 30S ribosomal subunits and not from a mutation resulting in a change in a ribosomal protein. Resistance to streptomycin and to several other antibiotics, of course, results from a change to ribosomal proteins. Following up this discovery, important not least because it at last provides a handle on the question of the role of ribosomal RNA (*ibid.*, page 1), Helser, Davies and Dahlberg have now, as they report next Wednesday in *Nature New Biology* (January 5), determined the function of the kasugamycin A locus of the *E. coli* chromosome, the locus which controls whether or not a cell is resistant to the antibiotic.

Knowing that the 16S ribosomal RNA from resistant strains of *E. coli* lacks the dimethyl groups which are normally present on two adjacent adenine residues near the 3′ terminus of this molecule, Helser *et al.* set about trying to prove that the kasugamycin A locus specifies a specific RNA methylase. They found that extracts of wild type *E. coli* contain a methylase activity, not present in identical extracts of resistant cells, which, although it will not methylate naked 16S RNA from any source, will methylate the 16S RNA moiety of 21S ribonucleoprotein cores derived from the undermethylated 30S ribosomal subunits of resistant cells. Similar 21S cores from wild type 30S ribosomes are not, however, methylated.

To prove that it is the RNA rather than the protein of the cores that is being methylated and to prove that the methylation is specific, Helser *et al.* made fingerprint analyses of the resistant 21S cores which had been methylated *in vitro*. Sure enough the methyl groups had been added *in vitro* to the two adenine residues near the 3′ terminus. Moreover, they have been able to show that 30S ribosomes reconstructed in the test tube from ribosomal proteins and cores from resistant ribosomes methylated *in vitro* are active in protein synthesis and are sensitive, not resistant, to kasugamycin. It seems, therefore, that the kasugamycin A locus is the structural gene for a specific methylase and a mutation in this gene which inactivates this enzyme confers resistance to the drug.

NUCLEIC ACIDS

Complex Forks

from our Cell Biology Correspondent

IN the current issue of the *Journal of Molecular Biology*, two groups, Huberman, Kornberg and Alberts (**62**, 39; 1971) and Sinha and Snustad (*ibid.*, 267), report experiments which strongly suggest that the protein specified by gene 32 of bacteriophage T4 plays a structural part in the replication of T4 DNA. At least nineteen genes of phage T4 participate in the replication of its DNA. Gene 43 codes for T4 phage specific DNA polymerase which like *Escherichia coli* DNA polymerase requires a primer and uses as substrate the nucleoside tri-phosphates. Gene 32, on the other hand, is required in stoichiometric rather than catalytic amounts and must be present throughout the phage's replicative cycle. Alberts and his colleagues (for example, Alberts and Frey, *Nature*, **227**, 1313; 1970) have purified gene 32 protein and shown that it binds tightly and co-operatively to single stranded DNA. They have suggested therefore that the role of this protein is to denature double stranded T4 DNA and so provide the aligned, parental single DNA strands required as template by the T4 polymerase. The experiments which Huberman *et al.* report are certainly consistent with that picture.

Huberman *et al.* find that *in vitro* gene 32 protein stimulates by some five to ten-fold the rate of DNA synthesis by T4 DNA polymerase programmed with single stranded T4 DNA. Moreover, this stimulation *in vitro* by a temperature sensitive gene 32 protein is temperature sensitive. The stimulation does not result from an increase in the rate of chain initiation and it is greatest at low temperature, at high ionic strength and when enough gene 32 protein is present to saturate the template DNA. These findings indicate to Huberman *et al.* that the protein most probably acts *in vitro* by eliminating regions of secondary structure formed when the template single stranded DNA chain imperfectly base pairs with itself; such secondary structures are presumably inhibitory to the T4 polymerase. There is also the possibility that some specific interaction between gene 32 protein and molecules of T4 polymerase is involved in the stimulation because in the absence of DNA the two proteins interact to form a weak complex.

Sinha and Snustad (*ibid.*, 267) have ingeniously exploited a gene dosage experiment to show that *in vivo* the role of gene 32 protein is stoichiometric rather than catalytic. They infected amber restrictive *E. coli* with mixtures of various proportions of wild type T4 phage and strains carrying an amber mutation in gene 32. In such infections the rate of T4 DNA synthesis and the burst size falls off rapidly as the proportion of wild type phage is decreased. In other words, the number of copies of functional gene 32 protein present seems to determine the rate of T4 DNA synthesis and hence the burst size.

Together with the data reported by Huberman *et al.*, Sinha and Snustad's findings lead to the conclusion that the T4 replication fork contains, in addition to, indeed in advance of, the T4 DNA polymerase, a run of gene 32 protein molecules bound to the template DNA. And according to the calculations of Huberman *et al.*—because there are about sixty T4 replication forks in an infected cell and about 10,000 molecules of gene 32 protein—each fork must contain of the order of 170 gene 32 protein molecules. It might even be imagined that not until this run of gene 32 proteins has associated with the T4 DNA can replication commence.

NUTRITION

Effects of Alcohol

from a Correspondent

AT a symposium on alcohol in nutrition, organized by the Nutrition Society at the Middlesex Hospital Medical School, London, on December 3, the chairman, Professor Sir Charles Dodds, in his opening address stressed the importance of improving knowledge and understanding of the effects of alcohol in man, its use and abuse in society, and its role in nutrition and medicine. Professor F. Aylward (University of Reading) traced the history of the use of alcoholic beverages by man since early times in various societies and its consumption in different countries and noted that the consumption of wine had increased in the United Kingdom in recent years.

Dr G. L. S. Pawan (Middlesex Hospital Medical School, London) described the pathways of alcohol metabolism in man and his experiments to discover what procedures, if any, would significantly increase the rate of alcohol metabolism and "sober up" an intoxicated person. In his experience, intensive physical exercise, vitamins, caffeine or strong coffee, thyroid hormones and other substances are without effect, but of the sugars tested, fructose significantly increases the rate of alcohol metabolism and helps to "sober up" the intoxicated subject. Adaptation to a high fat diet, starvation for some days, and administration of 4-methyl pyrazole decrease the rate of alcohol metabolism.

Professor C. W. M. Wilson (Trinity College, Dublin) described some of the pharmacological actions of alcohol, and discussed the factors which affect the taste threshold of this substance in man. Mr J. C. McKenzie (Food and Drink Research Ltd, London) reviewed the important social implications of alcohol consumption. In his opinion, social rather than metabolic factors are the most important in the development of alcoholism.

Professor J. Tremolières (Hôpital Bichat, Paris) discussed the metabolic basis of ethanol toxicity. He presented evidence for an alternative peroxidase pathway of ethanol metabolism, not involving either the alcohol dehydrogenase nor the microsomal ethanol oxidizing systems, which in certain conditions may be important in man.

The Earth's Atmosphere and Quasar Redshifts

THE distribution of quasar emission line redshifts is intriguing because it can be used to support a wide number of ideas about the universe, depending on the assumptions used in its interpretation. But one assumption which is common to all attempts to use quasar redshifts as a means of probing the universe is that the effects producing the observed distribution are properties of quasars and their position in the universe. R. C. Roeder and C. C. Dyer point out in next Monday's *Nature Physical Science* (January 3) that this may not be a valid assumption, and that the Earth's atmosphere probably produces an "ease of measurement effect".

This work extends Roeder's earlier investigation of the origin of quasar redshifts (*Nature Physical Science*, **233**, 74; 1971). It seems that the effect is manifested by a tendency for more quasar redshifts to be determined for values close to existing humps in the distribution. It may be that these redshifts are simply easier to measure or, more subtly, that observers are more confident in announcing observations which have a superficial resemblance to results already in the literature. In their latest work, Roeder and Dyer lean towards the first view.

Night sky lines will probably have an effect on redshift measurements when the quasar spectra are shifted so that their lines are close to those of the night sky. One plausible example is the line CIV 1549 which could easily be shifted by redshift $z=1.61$ to interfere with Hg 4047 from the sky. The Hg lines are particularly significant in the spectra taken at the Hale Observatories and Lick Observatory, and OI and NaI are often seen in spectra obtained at Kitt Peak. Quasar lines should be more easily identified when there are many more quasar lines in the optical window than the number of night sky lines.

CHEMICAL SOCIETY SUPPLEMENT

The Amalgamated Societies

GEORGE PORTER

President of the Chemical Society

On January 1, 1972, some forty-two thousand chemists will become fellows of the Chemical Society which, although retaining its old charter, will assume a new role, uniting the membership of the old Chemical Society, the Royal Institute of Chemistry, the Faraday Society and the Society for Analytical Chemistry.

IT is often relatively easy to found new societies or new committees, and relatively difficult to dissolve or amalgamate them once they have been established. Thus, quite apart from borderline sciences such as biochemistry, pharmaceutical chemistry and chemical engineering, there had arisen, in Britain, five quite independent societies concerned with chemistry. To bring four of them together has involved five years of patient negotiation, in spite of the clearly expressed wish of the overwhelming majority of members of each of the societies to amalgamate. Although a referendum of members of the fifth body—the Society of Chemical Industry—showed that a majority of those voting were in favour of amalgamation, this society remains for the time being outside the principal body of chemists.

Case for Amalgamation

Why did more than 90% of voting members of the amalgamating societies think amalgamation desirable? There are many reasons; greater efficiency of operation, economy of staff and buildings, a wider range of services for members and so on. But there are two further reasons, more concerned with chemistry and chemists than with economics, which were perhaps more important in influencing their decision.

First is the divisive effect of quite independent societies representing the different branches of chemistry. One frequently hears of the gulf between the academic chemist and his industrial counterpart and this has not only been reflected in the different membership and activities of the five societies but, it could well be argued, has been exacerbated by this very separation of the societies. Furthermore, the division of chemistry into separate disciplines such as physical and organic and analytical is more noticeable in Britain than in countries such as the United States and can hardly be conducive to the development of a subject where these distinctions have become artificial and the inter-disciplinary areas are often the most fruitful.

The second reason why a society of all chemists is desirable has become increasingly apparent during the past few years and even during the course of the negotiations. Chemistry is now the concern of everyone because it has an impact on all our lives. It is a recognized profession practised by a large number of people and it is one of the principal subjects taught at nearly all levels of our educational system. The public rightly expect to be advised by the profession on all matters where chemistry affects their lives—on the chemistry syllabus for schools and universities, on the use of natural resources and the products of chemical technology. They also expect the scientist to explain and interpret his work to the non-scientist and to become involved in the problems of protection of the environment. Government departments are increasingly expecting scientists to explain and justify their requests for financial support. And the chemists themselves, concerned about the conditions of employment—or unemployment—are expecting their professional body to study and advise on these problems. All these things are matters for the chemistry profession as a whole, and can be dealt with most effectively by an organization which speaks for all chemists.

The disadvantages of amalgamation are chiefly ones which could arise because of sheer size. No one wants to see the unique discussions of the Faraday Society or the effective meetings of the specialist groups turned into large conventions where communication is possible only by one-way audio-visual aids.

Another, newer and at present rapidly changing argument against a single society is concerned with the wishes of many chemists that their society should play a greater part in professional matters, in negotiation of remuneration and conditions of service and the feeling of others that this is, perhaps, not the business of a learned society. The polarization of these attitudes has reached the stage in our sister society in America that it is one of the principal points at issue in the election of their president.

The form of amalgamation which has been agreed has, to a large extent, avoided these possible objections.

Structure of the New Society

The amalgamation of the four chemical bodies in this country on January 1, 1972, will not be a complete one because the Royal Institute of Chemistry will continue to exist with its own president and council. This is a source of disappointment to many members of all the societies. It arose in the first place because complete amalgamation would have required the negotiation of a new charter and, perhaps, the loss of privileges allowed by the existing charters of the Chemical Society and of the Royal Institute of Chemistry. Although full amalgamation under a single charter is still the wish of most fellows, it is also clear that, in the present state of uncertainty about the Industrial Relations Act and similar matters, the flexibility given by the two charters and the separation of professional from other matters, may be very valuable.

Sir James Taylor, who was chairman of the joint negotiating committee of the four bodies, has summarized the scheme of amalgamation as follows:

"The essence of the scheme is that the memberships of the Chemical Society (CS), the Royal Institute of Chemistry (RIC), the Faraday Society (FS), and the Society for Analytical Chemistry (SAC) shall unite into one society on a basis of equality. This can be brought about most advantageously by using the CS Royal Charter as instrument for the union. All members of the participating bodies shall have the opportunity of becoming Fellows of the Chemical

Society which in its 'new' form will be responsible for all activities other than the strictly professional and qualifying ones of the Royal Institute of Chemistry . . . it was decided that these activities must remain separate and be the sole responsibility of the Royal Institute of Chemistry in its modified rôle."

The character of the participating bodies is preserved in the amalgamated society by the establishment of six powerful specialist divisions and every fellow of the society is entitled to belong to two of the divisions and may join additional divisions for a small extra payment. The Faraday Society and the Society for Analytical Chemistry become the Faraday Division and the Analytical Division, while the organic and inorganic activities of the old Chemical Society come under the new Perkin and Dalton Divisions.

The educational activities which have until now been in the hands of the Royal Institute of Chemistry will continue, after amalgamation, under the Education and Training Board of the Chemical Society but an important feature is the formation of the Education Division. Now for the first time there will be an opportunity for any member of the amalgamated societies interested in chemical education to participate in developments both at secondary and tertiary levels. Much of this work will be done through subject groups dealing with the three basic areas of chemical education: curriculum reform and development, the production and use of educational techniques, and the appraisal and development of assessment methods. The division will encourage regional activities and will also organize meetings nationally. Awards and prizes for meritorious work in chemical education will be made by the division. Naturally there will be cooperation with the Education and Training Board, with the other divisions and with such organizations as the Association for Science Education.

The sixth division, the Industrial Division, is essentially a new activity of the combined societies and caters for the fact that more than 20,000 of the society's members are engaged in industry.

Each division has its own president and council and freedom to run the affairs of its own branch in its own way.

The council of the new Chemical Society includes representatives from the divisions and the RIC, and each divisional president as well as the president of the RIC is a vice-president of the society. The council also includes representatives of the regions in addition to members elected directly by the fellowship.

The staffs of the various bodies are already fully integrated, with the CS responsible for the provision of common services for the new organization except for professional matters and RIC charter activities which will continue to be managed by staff employed by the RIC.

This diversity within a single society is a unique factor of the amalgamation scheme which, we believe, combines the advantages of unity with the best features of independence.

Activities of the Society

All the old activities of the four amalgamating bodies are retained and the amalgamation creates new opportunities for promoting chemistry and relations with sister societies, with government, public bodies, educational and industrial organizations.

The Chemical Society and the Society for Analytical Chemistry have, for some time, encouraged the formation of specialist subject groups and this policy will be continued in the new society. Already thirty-eight subject groups are in existence, most of them affiliated to a division, but six of them are of interdivisional character. Several of the groups are operated jointly with other societies.

In the past, local activities have largely been conducted by the sections of the RIC, many of which have been in existence for more than fifty years. These activities will be continued and expanded by thirty-five local sections of the Chemical Society in Britain and Ireland whose function is to arrange local meetings and to appoint representatives to their regional committees which, in turn, nominate the regional members of council. The overseas local sections of CS and RIC will continue for the time being but an integrated structure is being worked out in time for operation next year.

In addition to meetings organized by local sections, by subject groups and by divisions, there are spring and autumn meetings of the whole society as well as several one-day symposia held at the Societies' Lecture Theatre in London and elsewhere. The fine rooms of the Chemical Society in Burlington House are open to all fellows six days a week and contain one of the most comprehensive chemical libraries in the world.

In addition, fellows who are also members of the RIC enjoy all the privileges of belonging to a professional qualifying body. Because membership of the professional body denotes a high standard of competence and the acceptance of a code of conduct, the members can expect in return to enjoy an appropriate level of remuneration and of status in the community; it is the principal function of the institute to ensure that this is indeed the case. As well as its activities on behalf of the whole profession—for example, by seeking to influence legislation—the institute provides help and advice to its members on an individual basis in connexion with their terms and conditions of employment and related matters. It also operates a very successful benevolent fund.

Publications and Information

The society has a very extensive range of publications, with a sales turnover of more than £1 million a year. *Chemistry in Britain* now becomes the house journal of the new organization and the *Journal of the Chemical Society* will be published in parts appropriate to each division, to be known as *Dalton Transactions, Faraday Transactions* Parts 1 and 2 (covering physical chemistry and chemical physics respectively) and *Perkin Transactions* Parts 1 and 2. *Chemical Communications, The Analyst* and *Analytical Abstracts* will continue as before. *Quarterly Reviews* and *R.I.C. Reviews* will be amalgamated to form *Chemical Society Reviews. Annual Reports* will be continued and the *Specialist Periodical Report* series will be extended. The Analytical Division will also issue two annual reviews on *Analytical Sciences* and *Analytical Atomic Spectroscopy. Education in Chemistry* will continue to appear in six issues a year and the popular RIC *Monographs for Teachers* will be expanded.

The Chemical Society has led the way in this country, through the United Kingdom Chemical Information Service, by supplying to its members and others a series of computer-based information services to help all those using chemical information to stay aware of published original work pertinent to their specific interests. Through an agreement with the American Chemical Society, UKCIS receives all the magnetic-tape files generated by the Chemical Abstracts Service in the United States and, at the same time, undertakes the supply to the Chemical Abstracts Service of abstracts and indexing terms for all primary British chemical literature in a form ready for incorporation directly into the computer data-base of the Chemical Abstracts Service. An outstanding capability for putting in and extracting information from a computer has been developed at the UKCIS centre at Nottingham University and major assistance given to the development of a world system of computerized scientific information.

The Chemical Society, in its new role, is therefore in a very strong position to serve chemistry and the chemist. Amalgamation has taken place at a time when the chemist is expected to accept a greater involvement in the continuing debate on the proper use of his science. The amalgamated organization will be well prepared to meet this challenge.

A Century and a Half of Chemistry

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In this article Sir Harold Hartley describes some of the early growth of chemistry and of the chemical industry.

It was on February 23, 1841, that twenty-five chemists, thanks to the initiative of Robert Warington, met in the rooms of the Society of Arts in John Street, Adelphi, to consider forming a Chemical Society which held its first regular meeting there on March 30, 1841. Among the chemists was Arthur Aikin, a remarkable man. He was one of the founders of the Geological Society and a former secretary of the Society of Arts. His abiding interest in chemistry arose out of his early friendship with Priestley; he became the first treasurer of the Chemical Society and its second president, Thomas Graham being the first. The formation of the society came at a most opportune moment; all over Europe chemistry was making rapid progress to which Britain, chiefly through Joseph Priestley, John Dalton, Sir Humphry Davy, Wollaston and Michael Faraday, had made outstanding contributions. Dalton's atomic theory, the atomic weights of Berzelius and his atomic symbols and equations had provided the framework on which chemistry was to grow. The advance of organic chemistry came both from the synthesis of natural products and the study of their reactions with inorganic chemicals.

Early Days in Europe

Discoveries came rapidly from the laboratories of Dumas, Gerhardt and Laurent in Paris, from Liebig in Giessen, Wöhler in Göttingen, Mitscherlich in Berlin and Berzelius in Stockholm. Berzelius had an encyclopaedic mind and his genius for generalization had produced the concepts of isomerism, catalysis and proteins. His *Annual Report on the Progress of Chemistry* in each year since 1822 had made him the accepted arbiter but when the Chemical Society was being founded, his authority was challenged by the younger men and chemical theory was in a state of flux. New discoveries prompted new views and even the values of atomic and molecular weights were a matter of controversy. The founding of the Chemical Society brought together a group of able men whose meetings must have been lively and stimulating with the presence of Brodie, Graham, William Odling—Gerhardt's l'ami Odling—and Williamson, whose classic paper on alcohol and ether was so helpful to Gerhardt.

And there were in London in those years several outstanding young German chemists who joined in the discussions—Kolbe came in 1845 to infect the young Frankland with his interest in organic syntheses from simple molecules, Hofmann came in the same year to teach at the new College of Chemistry in Oxford Street and Kekulé in 1853 as assistant to Stenhouse at the Mint. Kekulé used to say that his theory of the structure of organic compounds and his hexagonal formula of benzene came to him in a dream on the top of an omnibùs between Islington and Clapham Road where he lodged. Chemical theory in the years between 1840 and 1860 presented many unçertainties and so the Chemical Society was a focus of discussion. As examples of the results of difference of opinion about atoms and molecules in Kekulé's *Organic Chemistry* in 1858 a whole page is covered with different formulae for acetic acid and the formula of water is written in four ways: H_2O_2, HO, H_2O, H-O.

By 1860 two men, Kekulé at Bonn and Cannizzaro at Genoa, saw that these conflicting views about chemical theory would prejudice its future and perplex the minds of the younger generation. So they determined independently to take action to try to clarify the position. Cannizzaro published a précis of his lectures—a beautiful logical analysis of knowledge—in the *Nuovo Cimento* of May 1858 but it did not attract much attention. It had to wait for the Karlsruhe conference.

Kekulé suggested to Weltzien at Karlsruhe that they should summon the first international meeting of chemists at Karlsruhe in 1860 to try to reach a common understanding about atoms and molecules, to define precisely the ideas conveyed by the words, atoms, molecules, equivalent, atomicity, basicity, formulae and to initiate a uniform notation and rational nomenclature.

They had preliminary discussions about procedure when Kekulé suggested that they should elect a fresh chairman for each day to avoid causing jealousy and to prevent too much power being put into the hands of one man. On September 3, 1860, 140 leading chemists from different countries met at Karlsruhe; Weltzien took the chair at the first session and welcomed the members. He proposed the appointment of Wurtz, Roscoe, Kekulé, Strecker and Schishkoff as secretaries. Kekulé then made an opening speech and his notes show that he failed entirely to give a clear objective to the conference, rambling from one subject to another and going far beyond the terms of reference set out in the letter of invitation. He then suggested the appointment of a committee—consisting of the secretaries and additional members (including Cannizzaro and Kekulé)—to propose subjects for discussion the following day.

The first meeting of the committee revealed a fundamental difference of opinion between Cannizzaro and Kekulé, as Kekulé would only accept the evidence of chemical reactions about molecular and atomic weights and would not accept physical evidence which Cannizzaro had relied on extensively. It was agreed to pose the following questions for discussion by the conference. First, was it convenient to distinguish between atoms and molecules? Second, could the term compound atom be replaced by the expressions radical or residue? Third, was the idea of equivalents empirical and independent of the idea of atoms and molecules?

Boussingeult was in the chair at the second session of the conference and, as he himself pointed out, he was more familiar with applied chemistry than with theory. He protested at the view that the conference was to seek to reconcile the old and the new; as he said, chemistry does not grow old but chemists do. Kekulé then spoke to the first question and insisted that the magnitude of the chemical molecule could only be determined by chemical evidence and that physical methods were not acceptable; he quoted sulphur as an example. Cannizzaro opposed this view by saying that differences between chemical and physical atoms were unsupported by evidence. Discussion then followed on questions of notation and "barred atoms" and finally it was agreed to put the following questions to the final session of the conference. First, was it desirable to make chemical notation conform to the progress of the science? Second, was it desirable to adopt anew the principles of Berzelius with some modification? Third, was it desirable to distinguish by certain signs the new chemical symbols from those in use fifteen years before?

At the final session Dumas was again in the chair and Odling replaced Roscoe as one of the secretaries. Dumas opened with a long speech suggesting that there were two chemistries, inorganic and organic, and that the older equivalent weights should be used in the former and the new ones in the latter. This roused Cannizzaro to violent opposition of the idea that there were two sets of atomic weights and he was supported in this by Odling. Cannizzaro spoke at length of the value of Gerhardt's system, based on those of Gay–Lussac and Avogadro.

There followed a long discussion on the third question which was finally committed to the chairman who decided in favour of the use of barred atoms. Dumas then thanked the organizers and hosts of the conference, which ended, as Lothar Meyer said, without any conclusion, useful as it had been in the exchange of opinions. Stock comments that they must have separated in an icy mood.

But that was not the end, as Pavesis distributed copies of Cannizzaro's article in *Nuovo Cimento*. Lothar Meyer read his in the train on his way home and wrote, "I read it again and again and I was amazed by the clear light which that little paper threw on the subjects of our debates. Scales fell from my eyes, doubts disappeared and a feeling of certainty took their place. If I was able to help in clearing up the points at issue and cooling the hot tempers, I owe much to Cannizzaro's pamphlet. . . . The tides of battle began to ebb and the atomic weights of Berzelius once more came into their own". Four years later, in 1864, Lothar Meyer published his *Modernen Theorien der Chemie* which helped so much to clarify chemists' views about atoms and molecules.

Mendeleev, who also had a copy, wrote of it in some unpublished reminiscences. "The decisive moment in my development of the Periodic Law was in 1860 at the conference of chemists at Karlsruhe in which I took part and at which I heard the ideas of the Italian chemist, S. Cannizzaro. I regard him as my immediate predecessor because it was the atomic weights that he found that gave me the immediate reference material for my work. I noted immediately that the modifications he proposed in the atomic weights introduced a new pattern into Dumas' groupings and it was then that I was struck by the essential idea of a possible periodicity of the properties of the elements with increasing atomic weight. I was still hindered by the incongruities of the atomic weights accepted at this time; but I was firmly convinced that this was the direction in which to continue my work."

So in spite of its inauspicious ending, the Karlsruhe conference, thanks to Cannizzaro, was destined to have a decisive influence on the progress of chemical theory.

Chemical Industry and Engineering

So far I have said nothing of the chemical industry and the birth of chemical engineering. The traditional methods of the alchemists were chiefly used in the production of the acids and alkalines needed by industry and the extraction of sugar and dyes from plant products. The Napoleonic wars were making heavy demands for gunpowder and Lavoisier, having seen the inefficient methods used by the contractors, persuaded Turgot to let him take over management of the French Arsenal. He lived there and his notebooks show the detailed attention he gave to the collection and purification of nitre and its use in making gunpowder. His improvements increased the range of Napoleon's guns by 60 per cent. In three years he had a reserve of 5 million pounds of powder and his economies had amounted to 20 million livres. Lavoisier's work at the Arsenal was a fine piece of chemical engineering, making use of a combination of his expertise in science and mechanical engineering. He had a young friend, Irénée Du Pont, the son of the physiocrat, whose interest in chemistry led to his becoming one of Lavoisier's assistants. He and his father were constitutionalists and they fought beside the Swiss Guard at the Tuileries before emigrating to America to escape the Terror. And there on the Brandywine River at Wilmington, Irénée Du Pont built the powder factory that was destined to become one of the great arsenals of the allied nations. Lavoisier gave it a tradition of research and it was there a century later than Carothers discovered nylon, a substitute for silk.

In Britain chemical industry had taken a firm hold and later in the nineteenth century a meeting between Ludwig Mond, John Brunner and Henry Roscoe at Manchester railway station to discuss the investment of their slender capital was a landmark in the history of chemical engineering. Roscoe advised them to buy the British rights of the Solvay process for making sodium carbonate. Some firms had failed to make a success of it but Ludwig Mond installed it near his home in Winnington and by his skill and constant attention overcame all its difficulties. I was told that for the first year nobody was allowed to turn a tap on or off without Mond's consent. His next success was the Mond nickel process in which the compound with carbon monoxide was used to purify nickel. Meanwhile United Alkali was operating in Liverpool and British Dyes under Lewinstein at Manchester; Castner Kelner was making chlorine and caustic soda on the north-east coast, while Nobel Industries under Harry McGowan had works in Scotland. (In 1926 they were all amalgamated to form Imperial Chemical Industries, under the direction of Ludwig Mond and Harry McGowan.)

Then came the war of 1914–1918, called the "chemists' war" because they contributed so much to it through explosives, poison gas and smoke.

The progress of chemical engineering during that war owed much to K. B. Quinan, an American chemical engineer. At the outbreak of war he was in Cape Explosives and was shooting lions in German East Africa. Captured by the Germans he claimed American citizenship and came by the first boat to Britain where he offered his services to Lord Monckton, the Head of Explosive Supplies. He was soon in charge of production and his dynamic character and skill as a chemical engineer quickly increased British production of explosives and propellents, and lowered costs. Many young men owe their training in chemical engineering to Quinan. After the war he returned to South Africa and applied his ingenuity to improving the method of growing grapes, thus strengthening an important Cape industry.

New Partners and New Horizons

On January 1, 1972, the Chemical Society will enter a new phase of activity when it goes into partnership with the Royal Institute of Chemistry, the Faraday Society and the Society for Analytical Chemistry. With the increase in the number of members to 42,000 and the added strength of its new partners, the Chemical Society is equipped to deal with problems arising from the increasing world population. This will entail demands for more heat and power, more food, more water and more materials of every kind. All these will present problems for the chemist to solve. I foresee, especially, demands on electrochemistry and on microbiological engineering. The Faraday Division will help with the first of these but the divisions in general will need strengthening in microbiology to meet the contributions which only microorganisms can make. The new strength of the society is a good omen for a future in which so much will depend on the chemists' contribution and on bodies like the Chemical Society.

Change in the Chemical Industry in the 1970s

JACK W. BARRETT
President, Industrial Division of the Chemical Society

Dr Barrett examines the likely development of the chemical industry during this decade. Any assessment of current and likely future trends must take into account the fact that the industry is not a unified whole; it comprises several principal sectors, each operating in a distinct manner. But the industry's most outstanding feature has, nevertheless, been dynamic growth.

THE worldwide output of the chemical industry during the past decade grew by 9 per cent each year, compared with 6 per cent for the whole of industry. Japan's phenomenal growth in the 1960s averaged 16 per cent a year and, in North America, the growth of annual output was 7.5 per cent a year.

This trend was reinforced in western Europe too. Here, the industry grew by 10 per cent in volume each year during the past decade. Synthetic fibres led the sectors with an average yearly growth rate of 19.4 per cent. Plastics increased in volume by 16.8 per cent a year; basic organics by 13.7 per cent and inorganics by 6.1 per cent. In terms of value, pharmaceuticals increased by 9.5 per cent a year. To finance this rapid growth, capital investment in chemicals in western Europe was absorbing 11.3 per cent of all manufacturing investment by the middle of the 1960s.

Chemicals manufacture was also a significant proportion of all manufacturing output in western Europe in the 1960s. By the end of the decade chemicals accounted for 9.7 per cent of all manufacturing output. Consumption, valued at $4,500 million, was 6.5 per cent of the gross national product. And it amounted to $122 worth of chemical-based product for every western European man, woman and child. This outlines the immediate past performance. What of the present decade?

Consolidating Positions

The dynamic growth of the past decade is unlikely to be sustained during the 1970s. Total gross national product is not expected to increase at any greater rate than in the past decade and, indeed, the first two years of the 1970s show a considerable reduction. Consequently chemical growth is likely to be no more buoyant and, because of market penetration already achieved, there will be less scope for replacing traditional materials.

In this environment, the larger chemical companies will continue to consolidate their predominating positions. The enormous capital investment sums required to compete on the large scales that now exist preclude inroads by smaller companies. On the contrary, there will be some continuing pressures, particularly in certain sectors, that will prompt even greater size. This trend has already become apparent and in the 1960s there was a very considerable consolidation of national groups in Europe, to such an extent that the top ten chemical companies in western Europe today represent about 50 per cent of total sales compared with about 33 per cent in 1966 (Table 1).

Table 1 Sales of the Ten Largest Chemical Companies in Western Europe, 1966 and 1970

1966 sales	$ million	1970 sales	$ million
ICI	2,390	ICI	3,510
Bayer	1,687	Hoechst	2,882
Hoechst	1,416	BASF	2,874
Montedison	1,352	Montedison	2,842
BASF	1,144	Bayer	2,602
Rhone Poulenc	1,076	AKZO	2,014
Shell	905	Rhone Poulenc	1,985
Hoffmann La Roche	669	Ciba Geigy	1,613
Solvay	565	Shell	1,318
Ugine Kuhlmann	551	Ugine Kuhlmann	1,153
Total sales	11,755		22,793
% of total chemical industry sales, western Europe ~ 33%			~50%

In Italy, there is one chief chemical conglomerate which links the Montecatini, Edison and ANIC chemical operations. In France, there are now only two principal groups —Rhone Poulenc and Ugine Kuhlmann. The industry in Germany has continued to be dominated by Hoechst, BASF and Bayer who have extended their operations outside Germany. This is also true of ICI in Britain. At the same time, the companies in the United States have continued to grow in their home market and have greatly expanded their operations in Europe. Similarly European companies are making a major attack on the United States market and competition on a worldwide basis has become intense.

Although this process of consolidating dominant positions will continue, there are likely to be fewer large scale mergers than in the past. In the present situation, the need to merge or acquire in order to attain a size comparable with the big league leaders is not so pressing. Today the top dozen chemical companies (worldwide) show little significant difference in size. Dupont is only a few per cent greater in size than ICI and there are a further ten companies which are almost its equivalent.

The principal companies in the chemical industry are already established. Though operating internationally, they are, by and large, essentially national in nature. In the near future, their growth is likely to result from further extension of their operations across frontiers rather than by merger with "foreign" groups of comparable size.

The future participation of large oil companies in the chemical industry, either indirectly or through collaboration with large chemical companies, remains difficult to assess. The chemical operations of Shell, for example, are already of a size to put it in the world league class.

Larger Plants and New Processes

Within the large established companies, however, the trend to large production units will continue to the detriment of the smaller ones. At the same time inflation in the cost of these plants will continue. This, together with the sheer size of necessary investment of large production units, will exert a considerable pressure within the industry to concentrate more effort on optimizing the efficiency of existing processes. The larger the unit, the more advantage that can be gained from a small percentage increase in yield. The risk entailed in a new process is greater today than it ever was.

This is not to say that new processes will not be introduced. They will, but they will be subject to even greater scrutiny and will need to demonstrate outstandingly better performance before superseding existing processes. The Sohio process for acrylonitrile is a good example of a new process which was almost impossible to deny for introduction on a large unit basis. This was not marginally but very much better than the previous process.

Manufacturing Sectors

As the chemical industry is extremely heterogeneous, an assessment of growth prospects can best be made through consideration of its chief sectors—synthetic fibres, plastics, basic organics and pharmaceuticals (Table 2).

Table 2 Chemical Industry—Sector Volume Growth in Western Europe

	Growth rate % a year	
	1960–1970	1970–1980 (estimated)
Basic organics	13.7	9
Inorganics	6.1	<6
Plastics	16.8	11 to 12
Synthetic fibres	19.4	8
Pharmaceuticals (value growth)	9.5	<9

Synthetic fibres are likely to expand somewhat more slowly during this decade than before but will still remain one of the largest sectors. Much of the remarkable growth in totally synthetic fibres—from 3 million tons worldwide in 1960 to 8.4 million tons this year—has been at the expense of natural fibres such as cotton, wool and cellulosics. In western Europe, synthetics' share of total fibre consumption rose from about 6 per cent to 30 per cent in the 1960s. It can confidently be anticipated that this inroad will continue, perhaps to reach about 50 per cent by the end of this decade (Fig. 1). Growth, however, is likely to be at a slower rate as traditionally supplied markets become more and more absorbed.

Plastics, also, have expanded very rapidly—twenty-fold in twenty years—but it will also be difficult to maintain this meteoric growth rate during the present decade. Perhaps the future annual rate of growth will be nearer 11 to 12 per cent rather than the 16 to 17 per cent that seemed to be the rule in the 1960s.

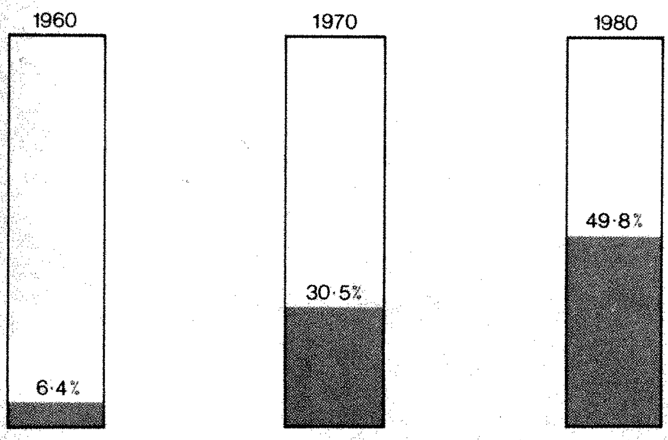

Fig. 1 Consumption of synthetic fibres as a percentage of total fibre consumption (western Europe).

Polymer science and technology are, however, still young and research will continue to extend knowledge and offer new opportunities. Therefore despite present profit difficulties polymers still offer the greatest scope for growth, not only because they are increasingly replacing articles traditionally made in metal, wood and glass, but because their innate potential for supplying existing and new needs is far from being realized at present. Improvement in the standard of living for more and more people will continue to increase demand for plastics in consumer goods.

Because the basic organic chemicals sector will continue to be the materials supplier for the synthetic fibres and plastics sectors, it must surely remain a very predominant part of the industry. Here again, though, it is unlikely quite to maintain its recent rate of increase.

Whatever influence social demands will have on plastics, they will have even greater influence on pharmaceuticals. Indeed the nature of the pharmaceutical sector is likely to be dictated more by social demands than any other sector. Increasing concern about the safety of drugs means that it takes longer and longer to screen, test and market new products. New products are not likely to emerge in less than five years from the time of their inception and the cost of development, including extensive biological evaluation, can be more than $12 million a product.

One inevitable result will be the introduction of fewer new drugs each year. This, in turn, will mean increasing the output of existing products to keep pace with demands from growing populations. There is, therefore, likely to be a fall in the rate of growth of the industry's money turnover because these older products command lower prices than new ones.

Pharmaceutical turnover worldwide now approaches $1,680 million and, in the past decade, grew in value in western Europe by 9.5 per cent a year. It is clear that companies hoping to remain competitive in the pharmaceutical sector on a world scale during the 1970s will have to be larger, probably as a result of merger or acquisition, if only to bear the increasing cost of research and development.

Overtaking GNP

Although these estimates for the chief sectors of the chemical industry are all below those of the past decade, they are still rates of growth far greater than the anticipated growth in gross national product for Europe of 4.8 per cent a year (ref. 1).

Social influences arising from environmental issues are among the imponderables that could have significant effect on all sectors of the industry. Recent governmental edicts on cyclamates and NTA, to cite just two examples, illustrate how plans and investment can be laid waste, sometimes as a result of far from conclusive evidence. What is certain is that the chemical industry is now spending, and will continue to spend, more and more money investigating the biodegradability as well as all possible biological effects of its new products. Spending on new and improved pollution control equipment at its plants is also an increasing recurring charge against profits. Monsanto, for instance, is spending some $110 million over three years to improve pollution control at its plants. All this will not make chemical products cheaper and, for the smaller organizations, may make the future even more problematic.

Any predictions for the chemical industry, based as they must be on present trends, cannot, however, assess the future results of its most potent asset—the fact that it is an industry essentially based on scientific discovery. New science introduces new opportunities. It can also eliminate old obstacles. Scientists, themselves, may yet set the most significant trends of all.

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[1] *The Growth of Output, 1960–1980* (OECD, Paris, 1970).

The Future for Chemistry

The late Professor Sir Ronald Nyholm, Professor M. Stacey and Professor J. W. Linnett give their views about the future development of the three traditional disciplines of chemistry.

RONALD NYHOLM

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MODERN inorganic chemistry may be defined as the integrated study of the synthesis and composition, the properties, reactions and structure of the chemical elements and their compounds, excluding most of those of carbon. Reaction studies include both thermodynamic aspects—equilibrium and heats of reaction—and investigations of kinetics and the inference of the mechanism therefrom. The term "structure" is widely interpreted as covering oxidation state, coordination number, stereochemistry and molecular conformation and deductions from the above and from thermodynamic data concerning the nature of the bonds present.

An important feature of the subject is the way an integration has been effected ; now, many of the so-called "topics" of inorganic chemistry have been woven into the fabric of the subject. Thus coordination or complex chemistry is no longer a topic to be treated separately but an approach to the whole subject.

What now of the future ? Prediction is at best a hazardous occupation but, although continual progress can be expected in well defined areas during the next few years, it is impossible to guess where an unusual development such as the discovery of ferrocene will take place. This, of course, is one of the exciting features of research. The continued application of known techniques, for example, ultraviolet spectroscopy, will continue to add to the understanding of energy levels in crystals and molecules. Newer techniques such as photoelectron spectroscopy and ESCA in which one can determine directly the energy levels of nonbinding electrons will help to increase the understanding of bonding in molecules ; X-ray crystallographic studies will continue to grow and indeed become almost the standard structural technique of "analysis" in the investigation of new compounds, at least where the structure is not obvious. Special attention is bound to be paid to the more accurate determination of bond lengths and bond angles to assist with the development of valency theory.

Synthesis of a purposeful kind will undoubtedly still occupy an important role in the future. But it will be more and more of the type which involves the use of ligands designed for the job and the preparation of compounds of the structure appropriate for the investigation in hand. The synthesis and study of "cluster" compounds such as $Rh_6(CO)_{16}$ and $[Pt_6Cl_{12}]$ has developed rapidly during the past few years and this is bound to continue especially with the use of different elements in the cluster (as in the carboranes). This provides a link-up between organic and inorganic chemistry. Inorganic chain type compounds are less common in organic chemistry but when it comes to clusters inorganic elements give rise to a wealth of derivatives containing many different atoms involving unusual stereochemical arrangements.

As far as structure is concerned, the principles governing the stability of what were formerly called "new or unusual" oxidation states are now so well understood that few oxidation states of the transition metals which are less than their Periodic Table Group Number remain to be "discovered". Similarly unusual coordination numbers no longer present an important challenge to the synthetic chemist but developments of a more subtle type will occur, for example, in the understanding of why some five-coordinate complexes are square pyramidal and others trigonal bipyramidal. It is to be hoped that knowledge of bonding will improve because topics such as double bonding and the nature of the link between metals and alkenes and alkynes still present many problems.

In the field of reaction mechanisms there is much to be done ; it is likely that the extension of the use of fast reaction techniques will help because when interpretation is possible they are often much simpler to interpret at least at the beginning of the reaction. The mechanism of formulation and reaction of organo-metallic compounds especially calls for detailed study. Fundamental advances are most likely to come from molecular beam experiments in the gas phase involving both organic and inorganic species. For the inorganic chemist working on compounds in solvents, a better understanding of the difference between inner and outer sphere reactions is badly needed. The nature of the solvation of ions and molecules still cries out for more investigation but chemists need a bright idea and, ideally, a new technique. The use of rates of reaction to enable chemists to draw conclusions about mechanisms of reaction will continue but it is clear that this still involves much intuitive speculation. One is tempted to suggest that deeper thought about what has been measured rather than a too rapid accumulation of new data would benefit the subject.

The accelerating development of biological inorganic chemistry is very likely. Promising advances have occurred recently, involving the synthesis of molecular nitrogen transition metal complexes and including examples of nitrogen fixation on a small scale, even at room temperature and atmospheric pressure. Although the fundamental understanding arising from this work is valuable and exciting, it is unlikely that ammonia will be synthesized commercially by such a process in the foreseeable future ; the chief industrial application will probably be the synthesis of organic compounds containing nitrogen formed by simultaneously coordinating and activating both nitrogen and the organic moiety at the metal atom.

Another area of biological inorganic chemistry which will continue to develop is metal enzyme chemistry, especially studies on metal complexes and their role as catalysts in biological systems. In spite of their importance in various biological processes including electrical impulse transmission, the understanding of the role of alkali metals in plants and animals is still very primitive. Recent work which has led to some understanding of the factors governing preferential coordination of potassium and sodium and other alkali metals is leading towards an appreciation of the reasons for the selectivity of sodium over potassium. The alkali metals have been shown to yield many unusual coordination numbers and stereochemical arrangements, but more work is needed on ligands more closely related to those found in living systems.

Undoubtedly, more research will continue to be done on the use of metal complexes as organo-metal catalysts for the synthesis of industrially important organic intermediates and polymers. Indeed, the most rapid progress in the developing field of organo-metallics is likely to take place in the use of complex metal compounds as catalysts for organic reactions. In addition to the precious (transition) metals already used for this purpose, for example, platinum, palladium, rhodium and ruthenium, there is little doubt that, by suitably designing the ligands attached to the metal, the more common metals—iron, cobalt and nickel—will find application in the same way as the precious metals (and copper). Much work at present involves the synthesis of a wide range of ligands with small variations in their properties and, as understanding increases, tailor-made polydentate groups will undoubtedly be possible.

Finally, in the industrial sphere, the design and use of suitable ligands for the preferential stabilization and extraction of metal ions, especially low-grade ores, should develop rapidly. Industry needs to make increasing use of ores containing much less than 1 per cent of the metal; decades ago, these would have been rejected from normal metal extraction processes as valueless. It is of interest to note that the recovery of metals like copper and tin from refuse and indeed even from "cheap" ores used for the isolation of other common metals like iron offers challenging fields for study. The use of continuous processes involving solvent extraction of coordinated metal ions will require the application of much of the knowledge about coordination chemistry acquired during the past two or three decades.

M. STACEY

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THE pace of organic chemistry is so rapid at present that it is bewildering and, because some aspect of it affects the everyday lives of all of us, too brief an account such as this may mislead, while to look very far into the future requires a whole team of science fiction writers.

By far the greatest activity continues to be in natural product chemistry where highly complex molecular structures are being unravelled and their syntheses accomplished. The great speed with which these researches are being achieved often arises from the employment of large teams of skilled research workers aided by a battery of physical techniques employing highly sophisticated instruments. For the extraction and separation of natural products there is electrophoresis (in many forms), ultracentrifugation, gel filtration, and so on, and for rapid and accurate identification of groupings and structures there is mass spectrometry, nuclear magnetic resonance and electron spin resonance. Optical rotatory dispersion and circular dichroism yield deep information on stereochemical situations, and the remarkable computerized X-ray crystallographic methods make available to the organic chemist complete structures of organic molecules. The number of new structures now reported in any one year is several thousand. Dramatic progress continues to be made on nucleic acid structures with the almost unbelievable total synthesis of a gene. Double-stranded helix biochemistry is giving way to more precise organic chemistry and it is becoming commonplace to synthesize molecules with seventy or more nucleotides in predominantly correct sequence and conformation. Likewise in the protein chemistry field quite remarkable sequences of amino-acids have been determined and syntheses, with the aid of "macromolecular catalysis" of huge block co-polymers with biological activity, achieved. Likewise carbohydrate giant macromolecules have had their structures unravelled and, as well as enzymic synthesis of these, a beginning has been made on chemical synthesis. New journals have arisen to report monthly progress in the fast moving carbohydrate field. Moving even faster is the field of organic fluorine chemistry—giving rise to several new specialist journals for its reporting and, with the advent of aromatic and heterocyclic fully fluorinated systems, having the potential for replicating every known organic compound with fluorine atoms replacing all or some of the hydrogen atoms.

New ideas have been propounded in every branch of organic chemistry, for example in the case of terpenoids, steroids, alkaloids, alicyclic and heterocyclic compounds and so on; with the help of the Hoffmann-Woodward rules, beautiful stereochemical syntheses of great importance have been made. Reaction mechanisms continue to be studied and molecular orbital theories and free radical reactions are now coming fully into their own.

Because something of the future is now determined, even in academic circles, by financial pundits, great happenings must be expected in those organic fields with an applied flavour. Enzyme chemistry must be near the top of this list. Although industrial and financial rewards may be long in coming in this field, the excitement and challenge to the organic chemist are so great that the pace must inevitably increase. The prospect of having "biocatalysts" available for the syntheses not only of natural macromolecules, but for carrying out specific reactions on relatively simple compounds is indeed exciting.

Further into the future lies the challenging possibility of synthesizing these biocatalysts. The coupling of enzyme research with nucleic acid research on the coding system of genes and chromosomes for the whole of biosynthesis will soon be a reality even though coding and uncoding for complex polysaccharide molecules have scarcely been contemplated. A great future field of research is the unravelling of the complex protein/carbohydrate/fatty complexes of all kinds which are important in health and disease. Among the most important are those hormones of the pituitary gland responsible for the reproductive cycle, and so a complete understanding of all the chemical systems involved, particularly in the human being, is necessary if we are ever to have complete power to limit our kind.

In the same context, the necessity to feed the whole population is of growing urgency. Biosynthetic protein food is no longer a dream and the whole chemistry of food, food additives, food flavours and aromas on a world scale will present a challenge to tomorrow's organic chemists. Nutrition, food assimilation and the chemistry of "living on less" must also be an important problem for the future.

For those of our organic chemists who enjoy working in three dimensions and have exhausted the cubanes and adamantanes, there is a new world of molecular complexity in the catenanes, rataxanes, knots and loops. These are chiefly synthetic compounds with some counterparts in certain DNA molecules which will offer a real manipulative challenge for the future.

The chemistry of viruses and of all unconquered diseases, the chemistry of the brain and of behaviour, must all involve future organic chemists.

J. W. LINNETT

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I FEEL sure that nothing during this century will rival the effect that quantum theory had on physical chemistry. In my opinion successes in finding ways of dealing with many-body systems offer the greatest rewards in real terms. These must be achieved by inventing new models and by finding useful approximations which made it possible to treat ever more complex systems. The growth of the third generation of computers will contribute tremendously, but chemical systems can involve so many particles that, even with larger computers, the full effect will only be achieved if new simplifying models are invented as well. Liquids and solutions present similar difficulties as regards the description of their structure and the calculation of their properties. Molecules of biological importance, such as haemoglobin, are also very large and a full understanding of their behaviour will involve understanding interactions within the whole complex system.

Molecular biology, so called, is potentially an exciting field for the physical chemist. Important advances in these areas will also result from well-devised approximations, together with perhaps a judicious admixture of theory and empiricism. In this context the importance and interest of polymers, colloids and other macromolecular systems must be borne in mind. Precise treatments cannot conceivably carry chemists far in any of these fields during the next twenty years. Such treatments will have to be reserved for much smaller systems and much simpler interactions. Whereas such thorough and complete treatments are essential as a basis for the development of physical chemistry, conclusions having broad consequences probably will not appear in this area, although an added significance has been provided in simple systems by the growing interest in the upper atmosphere.

In the past fifty years there have been great improvements in the understanding of gas phase reactions because more and more about collision processes at the molecular level has been studied. In other fields, such as those concerning surface processes, the structure of non-stoichiometric crystals, new techniques and new instruments allow examinations to be made directly at the atomic and molecular level. The profits will be considerable and genuine advances should be possible. I am sure that new instruments and new techniques will continue to appear over the next two decades so that we can examine with increasing detail the processes involved and interpret them at the atomic and molecular level.

As far as chemical bonding is concerned, it has been rare to predict new structures successfully. For example chemists failed to predict the structure of the higher hydrides of boron even after the bridge structure of diborane had been proved. Likewise, prediction of structures for the new and variegated organo-metallic molecules has not been markedly successful; chemists have usually depended ultimately on X-ray diffraction measurements. It is certainly to be hoped that developments in the valency field will improve the ability to predict, or at least suggest, new structures rather in the way that the stability of $B_{12}H_{12}^{2-}$ was predicted.

At this stage, it is important to try to make an especially clear assessment of the effect of the computer during the coming years. For some simple systems it will prove possible to calculate what we need to know but, probably for the next twenty years at least, most chemical systems will be too large for exact treatment. Therefore it is vital that sufficient physical understanding be obtained from the numerical solutions of small systems so that the treatment of larger systems can be improved.

I think that, besides the continued appearance of new instruments, advances of the greatest potential can occur in the area of large and complex systems (many-body systems). Here the computer will prove helpful but new models (or approximations) will be necessary. Small systems will continue to receive a lot of attention and because of the appearance of new instruments and techniques there will be progress in the details of interpretation and description.

Histories of the Societies

Each of the bodies that will be brought together in the new Chemical Society has a distinguished history. Many of the well established traditions will be continued by the divisions of the new society.

Chemical Society

THE first meeting of the Chemical Society was held on March 30, 1841, at the Society of Arts (now the Royal Society of Arts) in John Adam Street, Adelphi, WC2. Some seventy-seven persons had given their support to the formation of the society, and these must be regarded as the original founder members. The first president was Thomas Graham, who held the chair of chemistry at University College, London, from 1837 to 1855. The original designation of the society was "The Chemical Society of London" but after seven years, during which time the membership had increased to more than two hundred, many of whom had no connexion at all with London, the need was felt for steps to be taken to obtain a Charter of Incorporation. The charter was obtained in November 1848 in the name of the Chemical Society. Similar bodies of a national character were founded elsewhere at much later dates. The Société Chimique de France was founded in 1857, the Deutsche Chemische Gesellschaft in 1867 and the American Chemical Society in 1876.

The moving spirit in the foundation of the Society in 1841 was Robert Warington, who held an appointment as chemist with Messrs Truman, Hanbury and Buxton. He became the first secretary, and the first treasurer was Arthur Aiken, a lecturer in chemistry at Guy's Hospital. Other founder members included Richard Phillips, a contemporary of Davy and Wollaston, William Thomas Brande, the successor to Davy as professor of chemistry at the Royal Institution, J. F. Daniell, C. G. B. Daubeny, Warren de la Rue, Charles Macintosh and John Mercer. Michael Faraday was admitted to membership in 1842.

In 1857 the government agreed to accommodate the Royal Society and the Linnean and Chemical Societies in the old Burlington House, which it had purchased in 1854. The present buildings known as Burlington House were completed in 1873 and these have provided a permanent home for the society for nearly one hundred years.

The charter of 1848 provided for the admission of fellows, associates, honorary and foreign members. The class of associate was later abolished. The early activities of the society were also concerned with publications, the establishment of a library and with the setting up of a museum and of a laboratory for research. The last two objectives were allowed to lapse, but in both publications and the library the interest and activities of the society steadily grew.

Royal Institute of Chemistry

As early as 1867 there were discussions among the fellows of the Chemical Society on the conditions of admission and there were moves to restrict membership to qualified chemists—or at least to set up a new grade of membership denoting a standard of qualification. After considerable discussion and the taking of legal advice, however, it was decided that such a development was not practicable and that a separate organization was desirable. Accordingly the Institute of Chemistry was founded in 1877 and incorporated under the Companies Act in October of that year, with Professor Frankland as its first president. It was reincorporated by Royal Charter in 1885 (a second charter in 1949 adding the title "Royal").

There were initially two grades of membership—associateship and fellowship—and 255 fellows were elected as founder members in 1877. Examinations for the associateship were held early in 1879, based on approved courses at several colleges, and these examinations (since 1956 leading to graduate membership) still continue. A high standard of competence was demanded—particularly in experimental work—and this has been a feature of the institute throughout its history. A non-corporate grade of student membership was added in 1889.

This system of examinations for the associateship, which were in different branches of chemistry, and of subsequent election to the fellowship continued until 1918. In that year the associateship examination was recast as an examination in general chemistry, and examinations for the fellowship were introduced in special branches of chemistry. Also in that year exemption from the associateship examination was granted for the first time on the basis of university degrees with first or second class honours in chemistry. In 1956 the fellowship examinations were discontinued, the fellowship again becoming a grade to which admission was by election, and the former associateship examination now led to graduate membership—a non-corporate grade. Associateship henceforth denoted more than a qualification and required at least two years of postgraduate experience. The most recent change in membership grades took place in 1962 when the licentiateship was introduced—a corporate grade denoting the standard of a good pass degree in chemistry together with a minimum of one year of post-qualification experience.

The institute also awards a research diploma at PhD level and three masterships — in chemical analysis (MChemA), in pharmaceutical analysis (MPharmA), and in clinical biochemistry (MCB). The MPharmA and MCB are operated jointly with other professional bodies. The mastership in chemical analysis is particularly important in that its possession is a statutory requirement, for example, for a public analyst in Britain.

Faraday Society

On June 30, 1903, a few scientists, all members of the (now defunct) Faraday Club, met at the Royal Institution, the home of Michael Faraday himself, and founded a new scientific society "to promote the study of electrochemistry, chemical physics, metallography and kindred subjects"; inevitably, it was named the Faraday Society. Its first secretary was F. S. Spiers, who originated the particular technique of scientific discussion for which the society has become so famous. During his twenty-three years of service, the society's interests began to turn away from the more technical aspects of its original objects and towards the broader, fundamental topics of physical chemistry. This change was greatly accelerated during the tenure of Spier's successor, G. S. W. Marlow; in particular, the Discussions became an international and truly characteristic feature of the society's activities. The Electrodepositor's Technical Society (later, the Institute of Metal Finishing) took over the metallurgical and electrochemical technological aspects and the Faraday Society stimulated the increasing interest in colloid science by the acceptance under its auspices of (Sir) Eric Rideal's Colloid Committee, which had been formed in memory of Sir William Hardy. In 1948, this emerged as the Faraday Colloid and Biophysics Committee, with wide and active representation from other societies; in 1951, the objects of the society were redefined: "to promote the study of sciences lying between chemistry, physics and biology". A few years later, the society promoted the creation of a separate Biophysical Society; but the colloid science interests remained and a Colloid and Interface Group, affiliated to the Faraday Division of the (new) Chemical Society, has already been formed.

The Faraday Society now becomes the Faraday Division of the Chemical Society; its council and officers retain the sole responsibility for future Discussions and Symposia, and all their traditional features will be faithfully maintained.

Society for Analytical Chemistry

The Society for Analytical Chemistry was founded in 1874 by a group of public analysts as a means of exchanging information on methods of analysis. As the use of analytical chemistry became more widespread the public analysts were joined in the society by other consultants and by analytical chemists employed by industrial concerns, and the original name of the Society of Public Analysts was modified to the Society of Public Analysts and Other Analytical Chemists. In 1954 the public analysts, although retaining their membership of the society, formed a separate association; at this time the name of the society was again changed so as to reflect its wider activities and it became the Society for Analytical Chemistry (SAC).

As a result of the amalgamation negotiations the SAC will, in effect, become the Analytical Division of the new Chemical Society from January 1, 1972, for a three year trial period, and will cater for members joining the Analytical Division who are not members of the SAC. The SAC will celebrate its centenary in 1974, and before the end of that year a final decision on complete amalgamation will be taken.

The objects of the division will be those of the SAC, that is, "to encourage, assist and extend the knowledge and study of analytical chemistry and all questions relating to the analysis, nature and composition of natural and manufactured materials by promoting lectures, demonstrations and conferences and by publishing journals, reports and books". The present very full programme of meetings, symposia and conferences will be maintained.

Much of the strength of the SAC lay in the activities of its sections (now known as regions) and subject groups; these will be maintained in the Analytical Division. The boundaries of the regions have in most cases been altered to correspond to the new boundaries adopted by the Chemical Society and their organization will continue as before. The SAC first introduced specialist subject groups in 1944; it now has eleven and one joint group with the Pharmaceutical Society of Great Britain.

Axiom and Process in Genetics

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This article, the substance of Professor Darlington's final lecture course to Oxford biologists in May 1971, reconsiders the premises on which genetics has been based in the past hundred years.

THE achievements of genetics in the past fifty years, both in analysing heredity and variation and in explaining evolution, present us now with the problem of using its principles as the framework of biology. Before we can do this, however, we have to turn back and look again at our underlying assumptions: no less so because some of these by their very success have acquired in the course of time an unquestionable status.

The dangers that arise from taking too seriously an axiomatic distinction between heredity, development and infection have long been evident. Common propagation by DNA was a prior property common to the three and capable of overriding their differences[1]. More strictly within the field of genetics we can recognize the opposition between the analytical and the integral approaches of Mendel and Galton. But to Johannsen, the mathematician, who crystallized our ideas in the terms gene and genotype, the contrast was not fundamental. To him analysis was what mattered and analysis worked with differences. Individuals which could be counted exhibited differences which could be measured. The genotype could be the sum of the genes[2].

It has only been with the understanding of the processes of development, through which one cell was connected by way of the chromosomes with one individual, that the evidence of differences could be seen as indirect and partly misleading. Today it remains that the genotype is still not the sum of any identifiable genes[3]. There is a gap which may be represented in theory by the breakdown of classical genetics[4].

Putting aside this difficulty for the moment, we may note that Mendel, Galton and Johannsen were agreed on the supremacy of the individual as the basis of their statistical studies. This prime assumption swept all before it when the history of the chromosomes in sexual reproduction was found to vindicate it. At an early stage, however, a contradiction might have been noticed.

In his most far-reaching speculation on the origin of sexual reproduction Weismann[5] had suggested that the evolutionary value of fertilization and meiosis lay in their exposing the variation of individuals to the effects of natural selection. But a little later Weismann made another far-reaching suggestion. It was that the material of heredity, the germ plasm, is continuous from generation to generation and therefore potentially immortal[6]. This second idea is better known than the first but even less attended to perhaps because its archaic terms are thought to have been superseded by the precision of genes and chromosomes.

Weismann's two proposals came long before their time but both have been vindicated. Take continuity. When we think on a small scale of mitosis or the chromosomes, or of the replication of DNA, we encounter permanence, kinship and connectedness as genuine tokens of heredity. When we think of this connectedness on a large scale we recall first the dismissal of Lamarckism; then we recognize evolutionary networks which we can express as genetic systems undergoing selection and adaptation. And these systems, with their chromosome behaviour and breeding habits, developmental relations and life cycles, we then find stretch back into the past and forward into the future beyond the individual[7,8]. They rest on a continuity both of the determinants and of the things, the structures and functions, they determine.

Yet always within these systems we recognize the discontinuity of individuals. The reasons for this are both objective and subjective. It was always necessary, as Weismann argued, for nature to be able to discriminate between individuals in their characters and properties. And it was equally necessary for nature's investigators to count individuals if the causes of heredity, its genetic relations, were to be made clear. That is how it seemed to Mendel and later to the Mendelians. Moreover, to all human beings our own individualities, each and several, are the one commonsense fact of life, the point at which the objective and the subjective coincide.

The contradiction between Weismann's two proposals was thus not a technical accident. It was a genuine contradiction between the continuity and the discontinuity inherent in the process of sexual reproduction.

This contradiction calls for mutual adjustment or adaptation. When we represent the whole breeding system diagrammatically we see that it has certain circular connexions through which this adaptation would naturally arise. For the breeding system depends on the reproductive habit of a group, adapted to its long or short range advantage. This habit is determined by the heredity, chromosomal and cytoplasmic, which is carried not just by individuals but by the group. Thus the breeding system is the agent of discontinuity, mainly chromosomal, through meiosis and fertilization. But through mitosis it is the expression of continuity, potentially unlimited (Fig. 1).

Now, the breeding system is not the subject of an adaptation of heredity to environment. It is something which, for the individual, is interposed between heredity and environment. And if we ask how it is interposed we must also ask how far we can separate the individual from his connexions; and how far he is a part of a genetic continuum. In evolution what are selected are both individuals and the connexions between them. Can we estimate the relative importance of the two? Surely not. For outbreeding exposes individuality, inbreeding conceals it: the result depends on the variables effective in each situation, like heredity and environment, or temperature and pressure. But to see this problem as a whole we have to look again at the genetic system.

Genetic Systems at Work

The genetic system is genetic because it is the body of genetic properties, processes, particles and structures responsible for the heredity and variation, breeding and reproduction, of a species. It is a system because all these properties and entities are connected: connected adaptively in evolution much as the individual members of the species are connected.

The heredity of genetic systems is based, we believe, on DNA, on the linear sequences of nucleotides. Their adaptation is based on natural selection, but it is a selection which transcends individuals. It is mutual as between its parts: gene system and chromosome organization, meiotic habit and breeding system, reproductive habit and life cycle, are the parts and they are all one. It is therefore only indirectly concerned with the environment which lies outside it all. And it is organized as a rule to generate a limited uncertainty[9] which is adapted to the

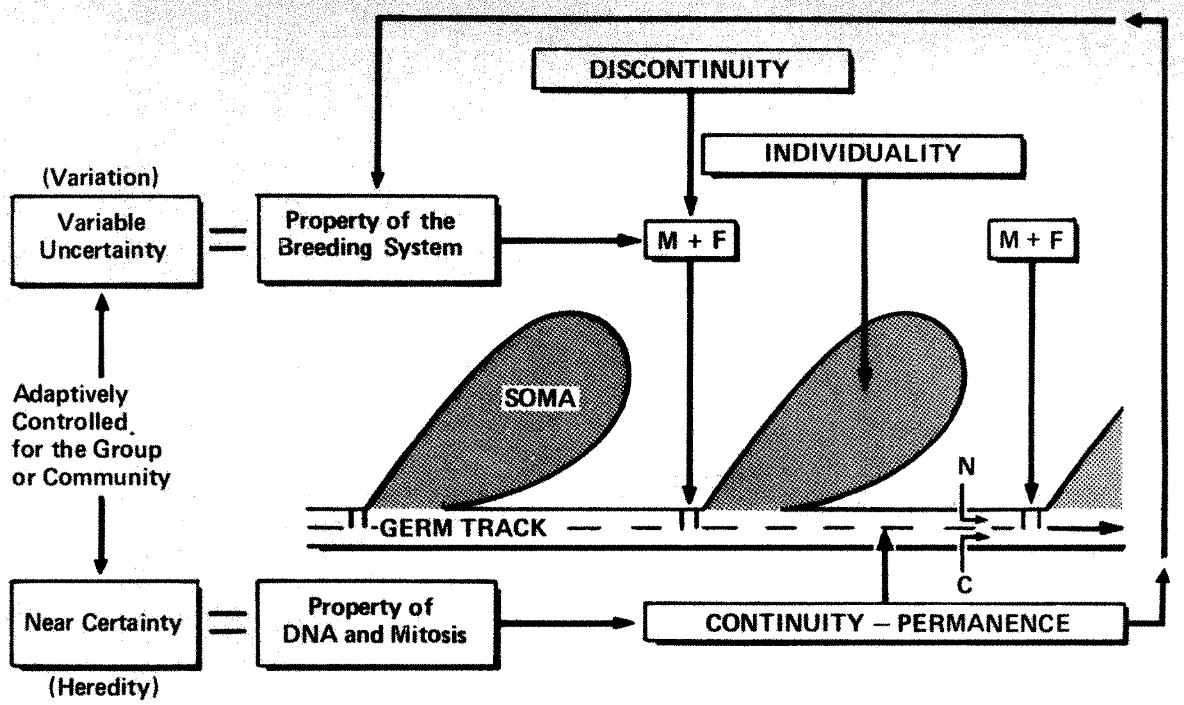

Fig. 1 The circular genetic relations underlying the antithesis between continuity and discontinuity in sexual reproduction. (M+F, meiosis and fertilization; N, nucleus; C, cytoplasm.)

past needs, and therefore, in some degree, to the future needs of the species.

Of the far-reaching connectedness of genetic systems we have many experimental examples. If a change such as polyploidy takes place at one point in a sexual genetic system its effects on self-fertility and cross-fertility at once change the size of the breeding group, the amount and value of recombination, the frequencies and effects of gene and chromosome mutations, the mechanisms of sex-determination and incompatibility, the selective value of balanced polymorphisms and so on.

If, on the other hand, in its geographical expansion a successful species penetrates new territories its success may depend on its ability to break down the very restrictions on inbreeding and outbreeding on which it has hitherto relied[10]. And the breakdown is likely to lead to an explosion of new forms in which meiosis and fertilization have their most formidable effects. For they can shatter the breeding system and probably the chromosome system along with it. In this way they may be able to create new species or even new classes of organism.

Thus with all its connectedness the genetic system in its continuous and successful evolutionary phase with sexual reproduction does not exclude either stagnation or revolution. The stable situations may be represented in a diagram of general connectedness (Fig. 2). They are what we see exemplified in the continuous fossil records with both directed trends and radial divergence. They correspond with the great systematic groups with constant chromosome numbers often stretching back, like the Gymnosperms, into the Permian or the Carboniferous[10]. And they correspond well enough with the classical experimental evidence from breeding within species in the period 1900 to 1925 on which mathematical evolutionists have so heavily relied.

Revolution, on the other hand, or repatterning[11] cannot be described in terms of stable systems or stable chromosomes. It is witnessed by the discontinuities and imperfections in the geological record which are still as obvious as they were to Darwin. But it is more precisely witnessed by sharp systematic discontinuities in chromosome sizes, numbers and behaviour, both in mitosis and meiosis, and in breeding systems such as haplo-diploid sex determination and the origins of style and endosperm in the flowering plants[12].

The violent contrast between regular and irregular processes in evolution compels us to face the inadequacy of the idea of laws of heredity and of evolution which have been favoured by physical analogies. To deal with this inadequacy we have to look at the chromosomes themselves.

Imperfectibility of Chromosomes

Genetics, since *Drosophila*, has generally assumed that the chromosomes obey the laws of heredity. They do what is required of them and do it well. Yet this is far from true. In sexual reproduction the chromosomes wrap up the genes in recombining bundles, perhaps one, perhaps five hundred. In a stable situation the difference does not matter. In an unstable situation it matters very much, for increase of numbers is easy but decrease is difficult. Gain of number thus means loss of adaptability: a blind alley.

Again the chromosomes recombine externally at meiosis by pairing and internally by crossing over. Both demand chiasmata. The relative importance of the two depends on the number of chromosomes. Hence in the whole sexually reproducing world we see the genetic system under stress to reconcile the needs of recombination between chromosomes and within them.

The most obvious evidence of stress is in two track heredity. The two kinds of meiosis responsible for the two lines of heredity and the two types of gamete are contrasted in distribution and frequency of chiasmata and crossing over. The classical example is *Drosophila* with suppression of crossing over in the male, the heterozygous sex. This situation with a novel type of meiosis is widespread in animals with a short life cycle[13]. It has recently been shown in hermaphrodite plants where crossing over, in general, is less frequent in the male line than in the female[3].

The genetic control of recombination is a universal problem in sexually reproducing organisms. It is dealt with not only in parallel in the two lines, but also in sequence by cyclical, obligatory or haploid parthenogenesis or subsexual reproduction. But with all these systems the chromosomes are being forced to do something which takes the species down an evolutionary blind alley.

Such species have taken the cash of immediate advantage and let the credit go. This is true whether it is a single parthenogenetic line of flies which has relinquished sexual variability and uncertainty and stereotyped a heterozygous condition[7,14],

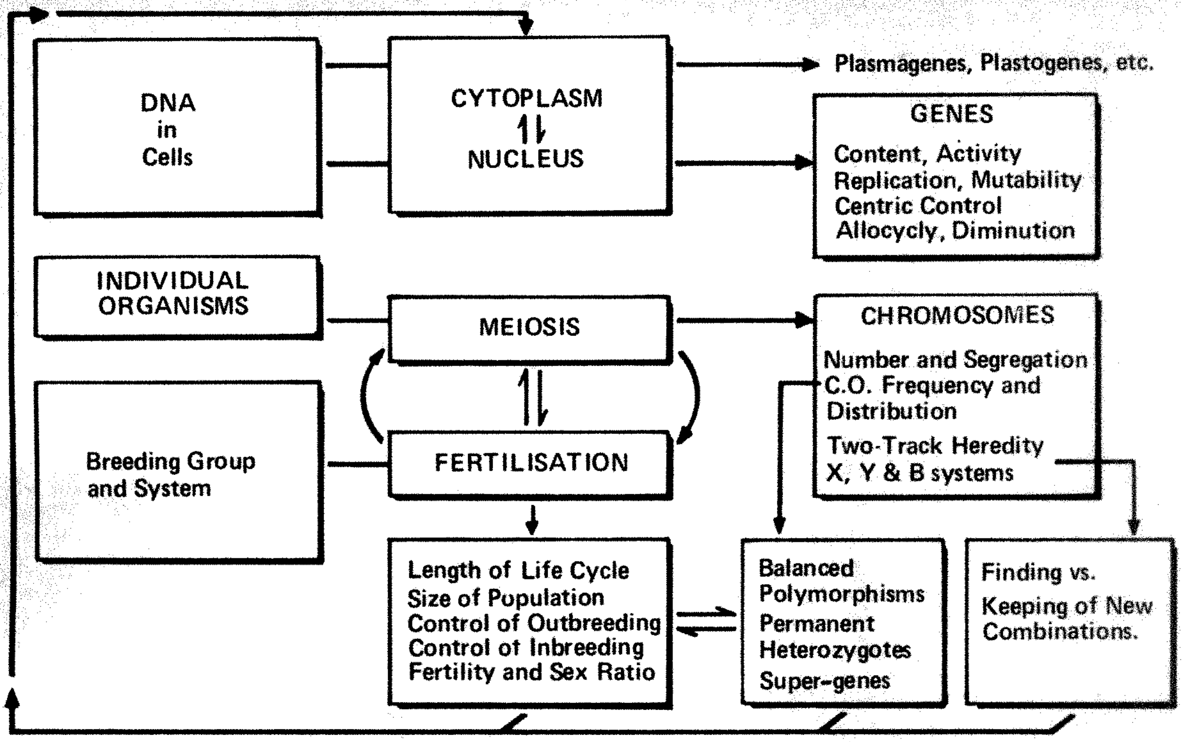

Fig. 2 The circular and reciprocal genetic relations underlying the evolution of sexual systems.

or the whole of the Hymenoptera, with their haploid males, whose success has been spectacular and prolonged. For these innovations, owing to their chromosome basis, are alike irreversible.

The same principle of imperfectibility applies to all sex chromosome mechanisms. Their repeated reconstruction has little relation to the sexual differentiation which they continue to determine. Their instability is the means by which they maintain stability in the species. It demonstrates the impossibility of regulating in parallel the variation of three kinds of chromosomes (*X*, *Y* and *A*) with different crossing over arrangements in their differential and pairing segments[15].

Again, the widespread existence of two types of chromosomes, the regularly recombining Mendelian *A* chromosomes and the irregularly segregating non-recombining non-Mendelian *B* chromosomes in short lived plants and insects[16,17], is an indication that the laws of heredity are not sufficient. And the chromosomes do not obey them.

Selection or Accident

The evolution of genetic systems we now see implies interactions, conflicts and compromises between the individual and the group, between heredity or continuity and variation or discontinuity. Our understanding of these throws light on the difference of opinion between Fisher and Sewall Wright. Theirs was a discussion of evolutionary principles limited partly by the assumptions of classical genetics and partly by the requirements of the mathematical models arising from these assumptions.

What was the controversy about? On the one hand, there was Fisher who wished to envisage evolution as something neatly deducible from the selective properties of separate genes. For him genetic systems had no existence except as physical systems. Even his own incipient idea of the evolution of heredity he allowed to be strangled by this treatment[18].

On the other hand, there was Sewall Wright who was willing to make less tidy assumptions about what happened in real life; indeed to admit the possibility of accidents tripping up the process of adaptation, accidents interposed at many levels between the gene and the organism[19].

What were these accidents? They arose from the genotypic control of mutation rates, choice and/or selection of environments subject to pre-adaptive variation[20,21]. Above all they arose from the sampling errors of small populations or more persuasively the founder effect[22].

On these bases, according to Wright, evolution might proceed on different lines in different groups and it might be either a fine-grained or a coarse-grained process. Here Wright was considering the chromosome evidence which had led me to argue that by origin and propagation there were six different kinds of species[23].

The great body of particular instances accumulated in the past forty years show us that the power of accident is not less but greater than Wright suggested. The diversity of processes and intricacy of their sequences he could hardly then have envisaged. Take the origin of the complex hybrid species whether in *Oenothera* or *Isotoma*. It arises, as experiments with *Campanula* and *Periplaneta*[4,24] have confirmed, through a switch of habit from outbreeding to inbreeding[25].

It occurs, as we should expect, in small populations isolated on the frontiers of an expanding species. This switch favours a change in the form of flowers which reinforces inbreeding and the genetic isolation and geographical mobility of small populations. It also favours the formation of non-recombining and true-breeding hybrids with interchanged chromosomes. The chromosomes of these hybrids come to be the vehicle of pairs of complexes which are separately lethal. They are mutually adapted in all their embryological relations, embryo sac, pollen grain, style, endosperm and embryo. These complexes exist because they are prevented from crossing-over and are genetically isolated from one another. The chromosomes of the same plant and the same cell are indeed (under pain of death) separated from one another as though poles apart. And their differences have become a balanced polymorphism recognizable, however, only in the haploid generation[4,14].

This sequence of inferences is not necessarily by any means complete. Yet so far as it goes it shows us how connexions interlock. It cuts across the terminology and brings together problems which evolutionists, who have confined their categories to genes and organisms, have always kept apart. It recognizes that, although the internal or genetic and external or spatial sources of isolation are separate and alternative[23], they interact immediately and in recognizable sequence. It recognizes further that a gene mutation such as causes cleistogamy or parthenogenesis can at one stroke separate a single individual genetically from the rest of the species and may therefore at one stroke become the origin of a new species.

The same kind of argument carried further recognizes a sound analogy between the inversions-plus-mutations which constitute a parthenogenetic species (such as *Drosophila mangabeiri*) and the similar constellation which kills Y sperm of males and constitutes the sex-ratio-modifying super-gene in *D. obscura*. Indeed, it rejects an ultimate distinction between the sex-ratio polymorphism in *D. obscura* and that in *D. willistoni* where a spirochaete kills the male embryos in the cytoplasm of the egg; where indeed an infectious particle has taken over the role of a gene-complex[14].

From this treatment two kinds of problem arise. One of these is quite practical. Our chief experience of super-genes or complexes comes from polymorphism. Can the polymorphic differential which binds a species be transformed into the species differential which splits it? Apparently not. In related species polymorphism continues for heterochromatin as much as for incompatibility[26]. And it is scarcely from a polymorphic super-gene that the control of meiosis in polyploid *Triticum* could be derived[27].

The other kind of problem is one of theory. It arises from an unreservedly genetic interpretation of events. For this interpretation assumes that heredity, development and infection are interchangeable manifestations of the activity of DNA. It accepts that the combination of genes with structural changes produces unique and unrepeatable discontinuities in evolution. It assumes that whether these discontinuities break up a species or hold it together is secondary since the two results may well follow from the same beginning.

To those accustomed to the classical statement of evolutionary problems in terms of genes deciding the properties of organisms this view may seem to violate the assumptions of Sewall Wright on small populations or the definitions of Ford on the treatment of polymorphism[28]. But are not these approaches now compatible with one another? For a small segment of chromosome may constitute a gene in the Fordian sense and situation. And the same segment by its original isolation may constitute a small population in the Wrightian sense and situation. To be sure these connexions are made at meiosis and they can be seen only under a microscope. And they can be accepted only by those to whom the properties of organisms, and cells and chromosomes, complexes and genes have an equal validity. Or to whom Samuel Butler's paradox that the hen is an egg's way of making another egg also has its validity[29].

Chromosome changes have one important property arising from their being identifiable in evolution by the hybridity which they generate. This is true whether it is interchange in *Oenothera*, inversion in *Drosophila* or polyploidy in *Triticum*. It is that they occur as sequences of events. And, as Haldane pointed out to me in 1928 (although it now seems obvious), each must in turn have conferred a selective advantage. What can be seen with chromosome changes must, however, be equally true of the sequences of invisible gene changes which play their part in the development of super-genes such as are responsible for incompatibility or heterostyly, for sex-ratio control, and above all for the patterns of instincts. Such long sequences all have a further common property inherent in them. It is that their separate steps although selectively advantageous do not reduce the selection pressure which favoured their origin. On the contrary they maintain or enhance it. There is positive feedback.

As *Oenothera* crossed America, or *Isotoma* Australia, or as the centipede, *Otocyrptops*, built up its chain of nine chromosomes, each interchange incorporated in the system made another interchange not less likely but more likely until the limit was reached. Such processes add up to directed evolution[22] or orthogenesis[30-32]. Ammonites and dinosaurs, the horse's foot and the giraffe's neck, give us the classical or absurd instances of this process but man's brain gives us an instance which can hardly seem absurd to us[33].

In their principle of positive feedback these examples are the same. But the fact that one is taken from the class of determinants that are still alive, the others from the class of organisms that are mostly dead, compels us to pay attention to their analogy. We notice that their sequences are irreversible. Feedback has taken control of evolution, hence what begins as progress acquires momentum and may end in disaster.

Heredity and Environment

In this evolutionary argument we have explicitly interposed a breeding system between the individual and its environment. The individual has lost status. How has it fared with the environment? The opposition between heredity and environment is taken as axiomatic for experimental organisms With individuals from populations in nature, with individuals which are not free from either the group or the system, does it work equally well?

The opposition between heredity and environment took shape in the hands of Galton and Johannsen. It was intended by them to apply where conditions on both sides, the inside and the outside of the fertilized egg and of the individual derived from it, could be defined by the experimenter. Success in making the distinction has been crucial for the advance of genetics. Failure has been the prime ingredient in concocting Lamarckian experiments.

The distinction has therefore come to be axiomatic. Yet at the moment of origin the axiom itself had been misapplied. The one-egg twins, the split eggs, on which Galton depended in 1875 for identity in heredity were found to differ. They differ through the act of splitting, an act which is inside the unsplit egg or embryo but outside its products. It is an act which creates a difference outside the ordinary processes of reproduction, a genetic difference which is not hereditary. The axiom is therefore not precisely an axiom[34].

Take now the evolutionary problem. We recognize the chromosome continuity between cells and between individuals. This is one kind of connexion. And with sexual breeding between all the individuals of the species we recognize another kind of connexion, that of the breeding system. But there are other connexions.

In the development of the egg, and in all cells derived from it, the cytoplasm is the environment of the nucleus. It is an environment with which the nucleus interacts; an environment which it may dominate, organize and differentially create. In doing so it creates tissues which act as a channel or filter between the outside and the inside of the plant or animal. The organism ceases to be homogeneous in its interactions with the environment.

Consider these interactions in vertebrate evolution. In its successive stages the relations of the nervous system with the rest of the body, as we know from the effects of gene mutations, become more complicated physiologically and genetically. In the mammals the relations of mother to embryo are prolonged and significant. The mother provides an environment which is no longer alien to the embryo. It is a genetic environment (Fig. 3).

We might suppose that this course of evolution is a mere physiological convenience. But if we look at plants this view is corrected. The higher flowering plants owe their character (and evidently their origin) to two modifications of the breeding system which are closely parallel to the innovations made by mammals. The angiosperms invented a style as a pollen filter. They use it to exclude pollen of a genetic character that is either too like or too unlike that of the mother[12]. Having let in the pollen, the apparatus of the egg has perfected a device which secures that the embryo shall have for its nutrition a half-sister, a dummy-embryo[35]. This endosperm is genetically intermediate between the embryo and its mother. If the parental chromosomes are M and P then the nutritive series in the ovule is MM, MMP, MP. In this way an exactly controlled genetic environment protects the new individual even from direct contact with its mother. The greater importance of

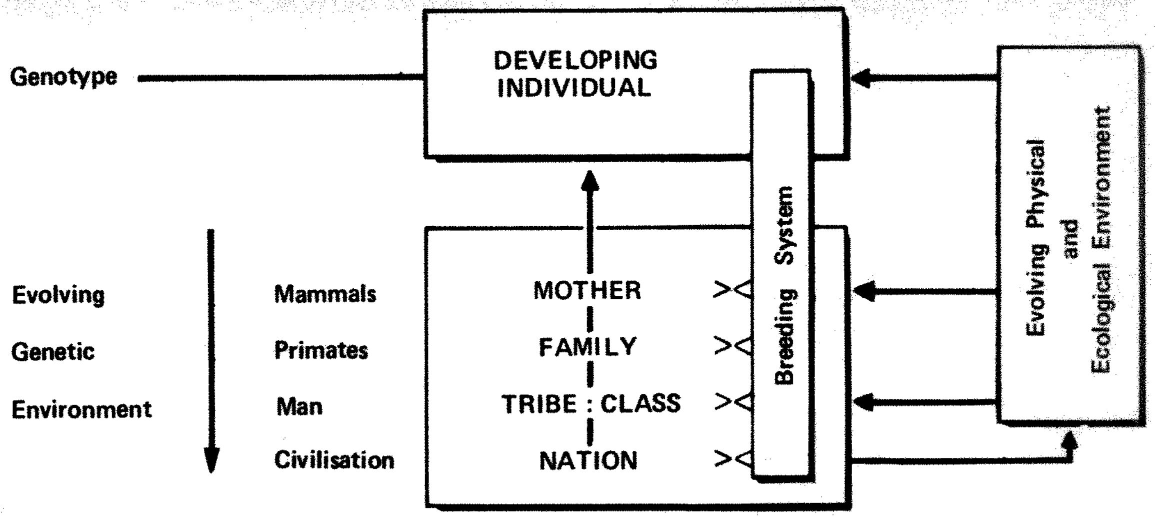

Fig. 3 The circular and reciprocal relations of heredity and environment underlying both human behaviour and evolution.

hybridization in the evolution of flowering plants than in any other group[11] is probably due to these two devices.

Returning to the mammals we see the genetic environment being extended with the evolution of the primates. As infancy is prolonged in man the child finds itself in an environment which includes not only a father, but a family, even an extended family, and a tribe. The relationships within the family and the tribe have their own intrinsic adaptations to the genetic system which has produced them. It is a system in which recombination at meiosis is adapted to the effects of assortative mating and the limitations of the incest taboo. It is a system which, in civilized man, has been carried to the length of creating castes and classes and nations, and within these it often allows of social mobility and selective migration.

In all these situations the environment has been diversified in parallel with the organism concerned, with the human species. In parallel for a good reason, namely that man himself has created the diversity of his own environments. And in stratified societies they are stratified environments. Not only in the human but now also in the physical environment of the individual man or woman there is a genetic component.

Here we see certain problems of earlier animal evolution reappearing in stylized form. Stability or instability in the environment is always important. But homogeneity or heterogeneity is also important and the homogeneous environment of the deep sea coelacanth in giving evolutionary stability represents the extreme contrast with the man-made heterogeneity of our human environments with their individual choice in mobility and migration.

Combination of Methods

Our understanding of biology has grown from the opposite ends of scientific method. It now seems that when the evidence from simple and rigorous experimental systems is brought together into one larger body of causal connectedness what seemed to be axiomatic assumptions become conditional and relative. And if the axiomatic view is continued it becomes dangerous. This is most obvious when genetics is put on an evolutionary time scale. For example, in the outbred heterogeneous society continuity is concealed, individuality is paramount. But in the inbred homogeneous society, individuality is concealed and continuity is paramount. Again within the individual the chromosomes govern heredity. But in evolution heredity also governs the chromosomes. Similarly, at any one stage of history man is seen as mastering and then creating his environment. But at the end of his history the environment he has created is seen to have been mastering him, a process which for genetic reasons is exceedingly difficult to reverse.

One of the reasons for these dialectical changes is of course the action of natural selection on the evolutionary time scale. Another is the fusion of the various biological and finally humane disciplines. These changes demand a flexibility of ideas and methods. Models which have been our servants have been taking control of us and have to be put back in their place. For these are not remote questions. They concern marriage and family, class and race, education and culture, health and employment, competition and population. And since above all they concern our attitudes to these problems they will affect the future of everybody.

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A New Approach to Pattern Recognition

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Automatic clustering methods are shown to provide a basis for adaptive pattern recognition when neither the number nor the specifications of classes are known in advance.

SOME terminology is needed to begin with. Descriptions of objects such as "red" and "2 cm long" are called attribute states and sets of attribute states such as "colour" and "length" are called attributes. The term classification is used for formation of classes of objects although many articles on pattern recognition use the term for assignment of objects to existing classes.

Present approaches to pattern recognition share the assumption that each of a set of classes to which new objects are to be assigned can be wholly or partially specified. In one approach it is assumed that each class is defined in terms of some list of attributes or relations. If, for example, a matching coefficient based on some set of attributes is defined on pairs of objects, each class may be defined as a neighbourhood of some typical object or template. A new object is assigned to a class if it matches the template closely enough. In the various structural methods of pattern recognition, images of objects are described by rules for assembling them from such components as line segments, curve segments, and corners (see, for example, refs. 1–3). Class definitions are given in terms of these structural descriptions. Similarly the methods for identifying parts of objects, devised by Jardine and Jardine[4,5], depend on the definition of classes of parts of different objects in terms of a set of relations that hold between parts in each object.

The classical statistical model of pattern recognition is applicable when classes cannot be defined in terms of some list of attributes relations. It is assumed that each of a set of classes $\omega_1 \ldots \omega n = \Omega$ has an *a priori* probability of occurrence $P(\omega_i)$ and is specified by a conditional probability density function $p(X s \omega\ )$, $i=1, \ldots, n$, over attribute states $x_1, \ldots, x_m = X$. If the costs of misidentification are equal, and an object described by X is observed, the quantities

$$P\ (\omega_i|X) = \frac{p(X|\omega_i)P(\omega_i)}{\sum\limits_{j=1}^{n} p(X|\omega_j)P(\omega_j)}$$

are computed and the object is assigned to the class ω_i for which $P(\omega_i|X)$ is greatest. This is the maximum likelihood assignment. Equivalently, the discriminant functions

$$g_i(X) = p(X|\omega_i)P(\omega_i)$$

may be computed and the class selected for which the highest value is achieved. When costs of misidentification are unequal, Bayesian or minimax assignment rules may be used.

In practice the probabilities of occurrence and the conditional density functions which specify the classes may not be fully known in advance and various strategies are used to learn the class specifications. In supervised learning, samples of objects correctly assigned to each class are provided. In unsupervised learning, it is generally assumed only that the objects presented are drawn at random from the classes $\omega\ , \ldots, \omega_n$ with probabilities $P(\omega_i)$ respectively. In both supervised and unsupervised learning, choice of a strategy depends on what is initially known about the classes. Thus if the form of the conditional density functions is known but their parameters are unknown, these may be estimated. Or if the discriminant functions are assumed to be linear, their coefficients may be learned. Statistical pattern recognition methods are reviewed in refs. 6–8.

The approach to pattern recognition which I suggest is nearest in spirit to statistical pattern recognition with unsupervised learning but it differs from all forms of statistical pattern recognition in two ways. First, no initial assumption is made about the number of classes and their specifications; second, it is not assumed that the objects encountered are drawn at random from some mixture of classes. These assumptions are inappropriate in many practical applications of pattern recognition. They may also be inappropriate in models for pattern recognition by higher animals.

The approach is based on the concept of seeking among objects systems of clusters in which members of each cluster are relatively isolated from members of other clusters. Methods for forming systems of clusters may be regarded as formalizations of the notion that formation of empirical class concepts depends on recognition of the overall resemblances of objects. The relevance of cluster methods to pattern recognition has been suggested by Sebestyen[9], Ball[10] and Duda[8]. Cluster methods have been widely applied to problems of classification in biology, psychology, sociology and so on[11,12]—the usual starting point is a dissimilarity (or similarity) matrix on the entire set of objects to be classified, which is based on the states of each of some set of attributes shown by each of the objects. The final product is a clustering of the objects which represents as accurately as possible their relative dissimilarities. In applying cluster methods in pattern recognition, objects are considered sequentially. The dissimilarities of each new object to the objects already clustered are used to place the new object in the system of clusters and, if necessary, to modify the system of clusters. In other words, cluster methods are carried out in such a way that cluster formation, diagnosis of new objects and modification of the system of clusters in the light of new information are performed by a single algorithm. This approach differs from statistical pattern recognition in that it is deterministic: each new object is definitely assigned to or excluded from each of the clusters already formed. It differs from the deterministic template matching and structural methods because it does not involve fixed definitions of each class in terms of some list of attributes or relations.

Systems of Clusters

We define a pairwise dissimilarity matrix d on a set of objects P as a real-valued function on pairs of elements of P, such that

$$d(a,b) \geq 0 \qquad \text{for all } a,b \text{ in } P$$
$$d(a,b) = d(b,a) \qquad \text{for all } a,b \text{ in } P$$
$$d(a,a) = 0 \qquad \text{for all } a \text{ in } P$$

In order to describe the systems of clusters to be considered, it is convenient to represent a dissimilarity matrix by a sequence of graphs, one for each of its values. The graph for value θ has vertices representing objects and edges joining pairs of vertices which represent objects which differ by θ or less. The single-link clusters specified by a dissimilarity matrix are the connected components of the graphs for each value of the dissimilarity coefficient (Fig. 1). The set of single-link clusters determined by a dissimilarity matrix on a set of objects constitutes a hierarchic stratified clustering of the objects. The level of a cluster is the least value of the dissimilarity matrix at which it appears as a connected component in the representative graph. Clusters at each level are disjoint and are nested in clusters at higher levels.

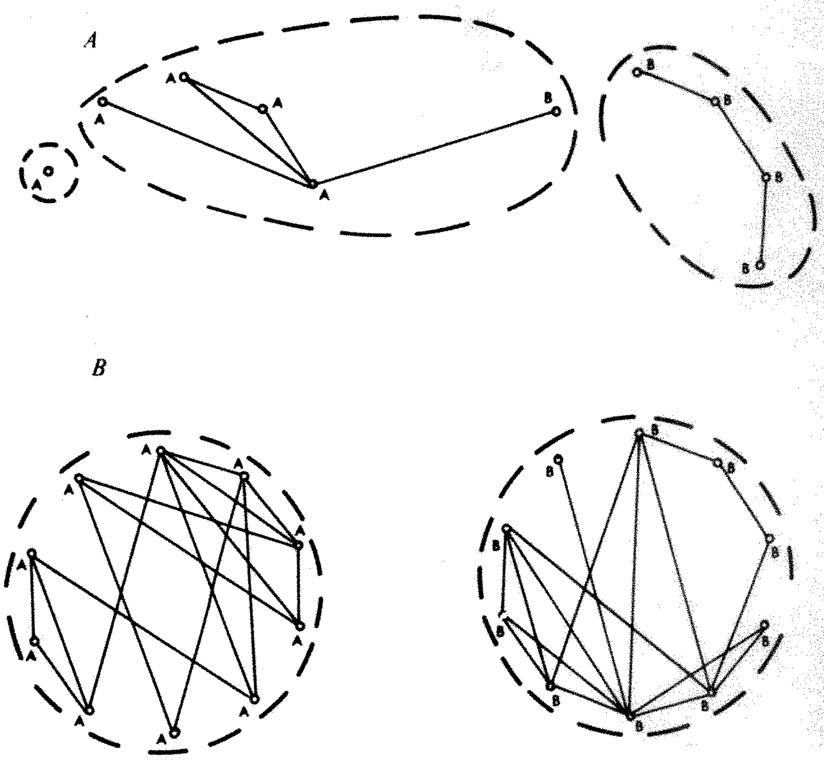

Fig. 1 *A*, Single-link clusters obtained when five untidily handwritten capital As and five Bs are clustered; *B*, single-link clusters obtained when five more As and five more Bs are considered. Vertices represent specimen letters and edges join pairs of vertices which represent specimens with dissimilarity θ or less, where θ is the cluster level.

The single-link cluster criterion has obvious intuitive appeal. Suppose, for example, that the objects considered are handwritten Roman capital As and Bs. It is plausible that from any one capital A it is possible to reach any other capital A through a chain of intermediate symbols each of which differs only to some small degree from the next, and each of which could definitely be identified as a capital A; it is also plausible that we cannot thus transform a capital A into a capital B without passing through a sequence of symbols each of which could not definitely be identified either as a capital A or as a capital B. If this speculation is correct, then the class of symbols of As and the class of symbols of Bs are single-link clusters specified by a dissimilarity matrix on the symbols of As and Bs. A more concrete example is taken from the analysis of pictures digitized by grey levels. If dissimilarity between cells in a picture is defined as a function of number of intervening cells and difference of grey level, then single-link clusters at some threshold of the dissimilarity matrix may represent images of objects or parts of objects in a picture (compare ref. 13).

The appropriateness of single-link clustering in pattern recognition rests, however, on the properties of the single-link cluster method as a method of data simplification, rather than on the intuitive appeal of single-link clusters. Jardine and Sibson[12,14] showed that the single-link method is the only hierarchic cluster method which satisfies certain invariance and optimality conditions. It is also stable in the sense that small changes in the values of a dissimilarity matrix can lead only to small changes in the resultant clustering, and it involves only order operations on the values of a dissimilarity matrix.

The single-link method may be inappropriate when objects intermediate between classes occur, because this can lead to amalgamation of otherwise well marked clusters; this can be avoided by generalizing the method to allow overlap between clusters. The k-link cluster methods[14], which satisfy the same invariance and optimality conditions as the single-link method, allow clusters to overlap by, at most, k–1 objects. To see how the methods can be used in pattern recognition it is necessary to consider the way in which the successive clusterings obtained by a k-link cluster method fit together as the set of objects clustered is extended.

Sequential Diagnosis

A diagnostic rule is said to be consistent with a method of classification if sequential application of the rule to all the members of a set of objects, in whatever order, yields the same system of classes as application of the method of classification to the whole set of objects.

The diagnostic rule consistent with single-link clustering is as follows. A new object is assigned to a cluster at level θ

if it differs by θ or less from at least one of its members. If a new object is assigned to more than one cluster at level θ then the clusters are amalgamated. If a new object differs by more than θ from all objects already clustered, it constitutes a new cluster at level θ. The diagnostic rule consistent with single-link is related to a rule, widely used in pattern recognition, which assigns each new object to the class of its nearest neighbour[15]. Use of the nearest-neighbour assignment rule presupposes, however, that a fixed set of classes is determined initially. The generalization of the single-link diagnostic rule to a rule consistent with k-link clustering is more complex (see ref. 14). It suffices to note that all the k-link cluster methods have an important stability property. Addition of a new object cannot alter the extension of a cluster at level θ if it is not linked directly, or indirectly through a chain of intermediate objects at level θ, to any member of the cluster.

The various average-link cluster methods which have been proposed as heuristics in pattern recognition do not have this property, so addition of a new object may alter the entire system of clusters. This property makes feasible algorithms which carry out k-link clustering by sequential diagnosis and hence perform simultaneously the operations of cluster formation, diagnosis and updating of a system of clusters in the light of successive diagnoses.

k-Link clustering by sequential diagnosis involves only order operations on the values of a dissimilarity matrix. In this it differs from most cluster methods and pattern recognition methods which involve such essentially algebraic operations as addition and multiplication. Pattern recognition methods which involve only order operations and which are invariant under order of presentation of objects may be of interest as models for pattern recognition by higher animals. Such methods could be carried out by simple threshold devices and could exploit redundancy in sensory input arising from repetition of kinds and arrangements of matter in the environment (compare ref. 16).

The construction of efficient computer algorithms to carry out k-link clustering by sequential diagnosis rests on the observation that once an object is assigned to a cluster C at level θ, its assignment to any cluster which includes C is guaranteed. It follows that usually only a small subset of the dissimilarity values between a new object and objects already clustered need be used to determine the position of the new object in the clustering. Van Rijsbergen[17] has described an algorithm which exploits this redundancy in carrying out single-link clustering by sequential diagnosis of objects or batches of objects. The algorithm can handle as many as ~1,000 objects.

Applications

I shall consider first an application in which the classes are known in advance. The objects are untidily handwritten Roman capital letters. Each is placed on a grid with its centroid at the centre of a system of concentric equally spaced rings, scaled so that the point furthest from the centroid lies on the outer edge of the outermost ring. Each specimen is described by the proportions of the occupied squares of the grid which lie within each ring. (The description is invariant under magnification, rotation, and translation of a specimen.) The dissimilarity between two specimen letters is the sum of the modular differences between proportions in corresponding rings. Other measures of dissimilarity are described in refs. 11, 12 and 18. Initially, when single-link clustering by sequential diagnosis is applied, the fit between the clusters obtained and the letter classes is poor but as the number of specimens is increased so the fit between clusters and letter classes improves. Fig. 1*A*, for example, shows clusters obtained after five As and five Bs have been considered; Fig. 1*B* shows clusters obtained after five more specimens of each have been considered.

In applications in which the classes are known in advance, clustering by sequential diagnosis is continued until a good or perfect fit between clusters and classes is obtained, or until addition of further objects produces no further improvement in the fit. Once a good or perfect fit is achieved, the clustering may be "frozen" by ceasing to allow amalgamation of clusters and creation of new clusters. Diagnostic rules which are much faster than the single-link rule may then be used. New objects may, for example, be matched with a typical object from each cluster and assigned to the cluster whose typical object they match best (see ref. 17).

The classes are not known in advance in such applications as the classification of documents to facilitate retrieval of documents relevant to requests. Each document is described by presence or absence of each of a list of keywords. Single-link clustering is applied to a dissimilarity matrix calculated from these descriptions. In ref. 19 it was shown that retrieval of documents based on matching of requests with document clusters is as effective as the usual strategies, which are based on matching of each request with each document, and is much faster.

When the classes are not known in advance it is more difficult to decide at what stage a clustering can be frozen. One approach is to define a measure of the extent to which a clustering is modified by diagnosis of a new object. As diagnosis of new objects proceeds, it generally happens that the average modification by each new object is initially high because new clusters are being created and existing clusters amalgamated. As the number of objects considered is increased, the average modification by each new object falls because creation of new clusters and amalgamation of existing clusters become less frequent. The clustering is frozen when the average modification falls below a chosen threshold. With a collection of 200 aeronautics documents, for example, it was found that the clustering ceased to be modified substantially after about fifty documents had been considered[19].

I conclude that clustering by sequential diagnosis is a useful approach to pattern recognition, especially when no initial assumptions can be made about the number and specifications of classes.

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Carbon Fibre Formation—the Oxidation Treatment

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This article describes analysis by infrared spectroscopy of the reactions occurring during the oxidation stage of the formation of carbon fibres.

THERE are two important steps in the production of high strength and high modulus carbon fibres derived from acrylic precursors: first, heat treatment while under restraint, in air at low temperatures (225° C) called oxidation, and second, heat treatment in vacuum or inert atmosphere at high temperatures (1,000–3,000° C). This is carried out in two stages, carbonization and graphitization[1]. The chemical and structural changes taking place during the oxidation stage are important with regard to the development of texture during the high temperature treatment.

Infrared Spectra

One important aspect is the part which oxygen plays in the thermal reactions. Research on this topic is hampered because the acrylic textile fibre normally used is 'Courtelle', which already contains oxygen in the comonomers, added to enhance its textile properties. So in a study of the oxidation reactions it is desirable to eliminate this complication by using a fibre consisting of the homopolymer, polyacrylonitrile. In the work discussed here, polyacrylonitrile was synthesized and spun into fibre form before infrared spectroscopy was used to follow the chemical reactions occurring during the oxidation step in carbon fibre production.

Infrared spectra were obtained by the KBr disk method on both polyacrylonitrile and 'Courtelle' fibres after heat treatments at 225° C, in air for various periods. This method proved rather unsatisfactory, and more sensitive spectra were produced from solvent cast films which were heated at 225° C in both air and nitrogen.

An assignment of the absorption peaks in the infrared spectrum of polyacrylonitrile has been made by Krimm and Liang[2]. The peak arising from the methylene (CH_2) group at 2.930 cm^{-1} is of particular interest as is that of the nitrile ($C{=}N$) group at 2,240 cm^{-1}. During thermal treatment, many new absorptions appear and develop in intensity, but unfortunately they tend to be very broad, which makes their characterization difficult. This effect may be the result of hydrogen bonding, several peaks overlapping, or because one type of chemical group becomes situated in several markedly different environments.

Spectral Changes

The inferences from the spectral changes occurring during the thermal treatment of polyacrylonitrile film in air may be summarized as follows: (1) The appearance and rapid growth in absorption at 1,590 cm^{-1} indicate the possible formation of $C{=}C$ or $C{=}N$ bonds or both, but the latter can be discounted in the early stages because the nitrile absorption at 2,240 cm^{-1} does not decrease initially. (2) Absorption in the 1,250 cm^{-1} to 1,150 cm^{-1} region indicates the presence of either $C{-}N$ or $C{-}O$ bonds but these two types cannot be distinguished separately. (3) After an induction period nitrile groups begin to react. Although the rate is linear at first, it soon decreases so that after many hours of heating, some nitrile groups still remain intact. (4) The environments of some nitrile groups (2,180 cm^{-1}) become more electronegative. These nitrile groups may take part in conjugation with the electronegative centres, for instance, the $C{=}C$ bonds referred to above. (5) The methylene group concentration (2,930 cm^{-1}) steadily decreases, eventually reaching zero. (6) The formation of OH and/or NH groups (3,330 to 3,230 cm^{-1}) are prominent reactions: their concentration steadily increases during oxidation. These groups become strongly hydrogen bonded. (7) The formation of carbonyl groups (1,710 cm^{-1}) occurs to a small extent although their first appearance is in the early stages of oxidation. (8) There is the possibility of the formation of

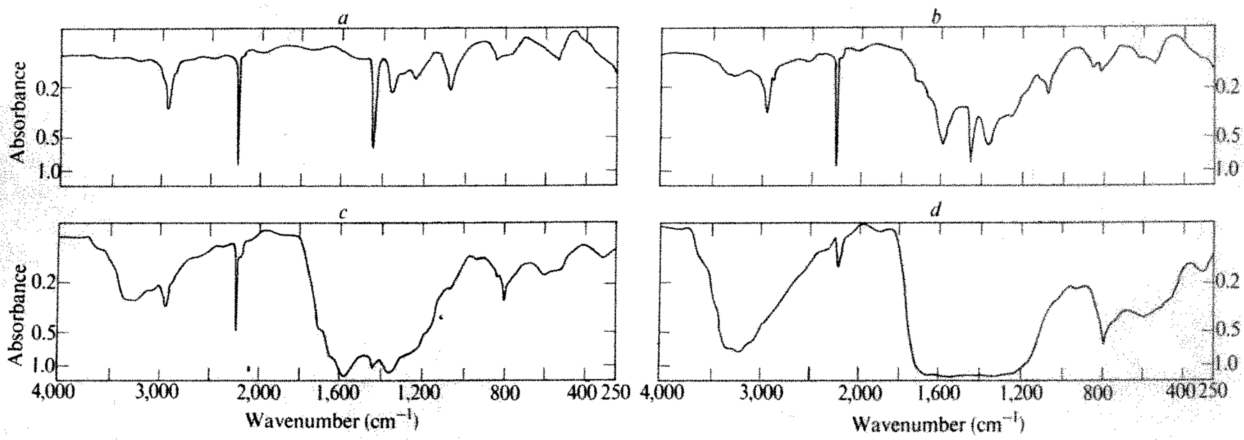

Fig. 1 Spectra of polyacrylonitrile film heated in air at 225° C for various periods. *a*, 0 h; *b*, 4 h; *c*, 10 h; *d*, 47 h.

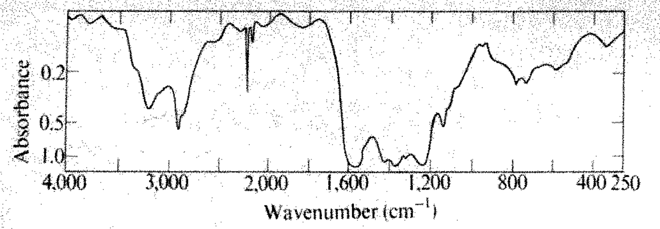

Fig. 2 Spectrum of polyacrylonitrile film heated in nitrogen at 225° C for 9 h.

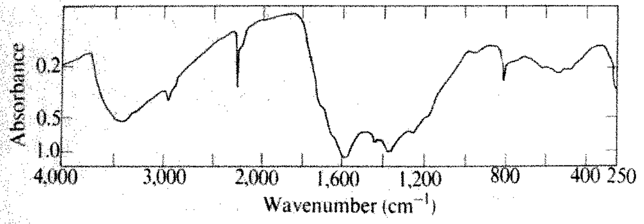

Fig. 3 Spectrum of polyacrylonitrile fibres heated in air at 225° C for 5 h.

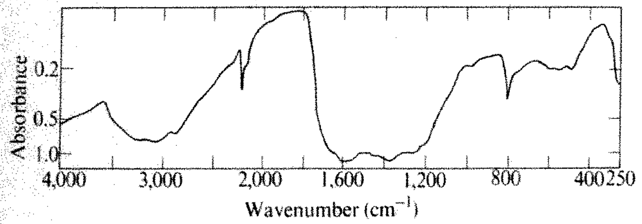

Fig. 4 Spectrum of 'Courtelle' fibres heated in air at 225° C for 5 h.

unconjugated and unsaturated centres (800 cm^{-1}) containing the C=CH group. This inference is subject to doubt because some cyclic compounds containing conjugated C=C and C=N bonds, for example, pyrimidines, exhibit an absorption, attributable to a ring vibration, in this region of the spectrum. Some of the spectra from which these inferences have been made are illustrated in Fig. 1.

The changes in the spectra when polyacrylonitrile film is heated in an atmosphere of nitrogen (Fig. 2) indicate, as expected, that carbonyl groups are not formed at all. But, more important, a large absorption at 3,200 cm^{-1} is still present, although now less broad, indicating that this absorption is caused by NH groups. If the assumption is made that the presence of oxygen does not alter the product of the cyclization reactions, these being considered separate from the oxidation reactions, we infer that the formation of NH groups is a major reaction during thermal treatment in air. It would seem from past work that NH groups are likely to occur at the end of cyclized sequences[3-5]. If this is so the presence of the large absorption caused by NH groups implies that only very short cyclized sequences are possible in the oxidized material. In fact, this has been concluded from thermodynamic measurements on polyacrylonitrile heated in inert atmospheres[6].

We expect the formation of OH groups to cause absorption in the 1,300 cm^{-1} to 900 cm^{-1} region because of the C—O stretching frequency, but this cannot be used for identification of the C—O group because the absorption due to the C—N group occurs in the same region. For the same reason, there may be other groups present containing the C—O bond, such as ethers and acids, which escape detection.

Comparing the spectra from film and fibres (Fig. 3) there would seem to be no qualitative difference in the reactions involved. Spectra produced by the KBr disk method on lightly treated fibres tend to be rather insensitive, because of the difficult grinding characteristics of these fibres, and sometimes a baseline shift is observed due to a radiation scattering effect.

It is, however, clear that the thermal reactions occur faster in the fibres than in the film, which suggests that they are diffusion controlled and the decrease in nitrile group concentration does not show an induction period.

The spectra from fibres also show that the reactions occur faster in 'Courtelle' than polyacrylonitrile fibres (Fig. 4). This may be caused by the comonomers used in 'Courtelle'. It has been found that copolymerized vinyl acids can initiate the cyclization reactions[7].

Chemical Structure

In conclusion the results of this analysis by infrared spectroscopy have indicated that the chemical structure of the oxidized 'Courtelle' and polyacrylonitrile fibres includes C=C, C=N, C—N, O—H, N—H, CH_2, C≡N (in at least two significantly different environments), C=O.

Although the spectra are unsuitable for accurate quantitative measurements, the qualitative indications are that the C=C, C=N, C—N, OH and NH groups are important constituents of the oxidized fibres, whereas the CH_2, C≡N and C=O groups are present only in small quantities.

Previous evidence has suggested that oxygen is present in the oxidized fibre mainly as carbonyl bonds[8] or bridging ether bonds[9] and a free radical mechanism for the oxidation reactions has been suggested[3]. This work has shown that in an adequately oxidized fibre the concentration of carbonyl groups is small while the formation of hydroxyl occurs to a significant extent, but there is no conclusive evidence for either the presence or absence of ether bonds. Also, the oxidation reactions seem to be diffusion controlled. The comonomers used in 'Courtelle' to enhance its textile properties appear to be beneficial for carbon fibre production in that they reduce the oxidation time. Most important, however, is the complicated structure of the fibre after the oxidation treatment.

Comparatively short oxidation times (approximately 5 h) are acceptable for the production of good carbon fibres, but it is clear from the work reported here that at such stages the fibres are only partially oxidized, and still contain significant quantities of nitrile groups attached to an aliphatic polymer chain,

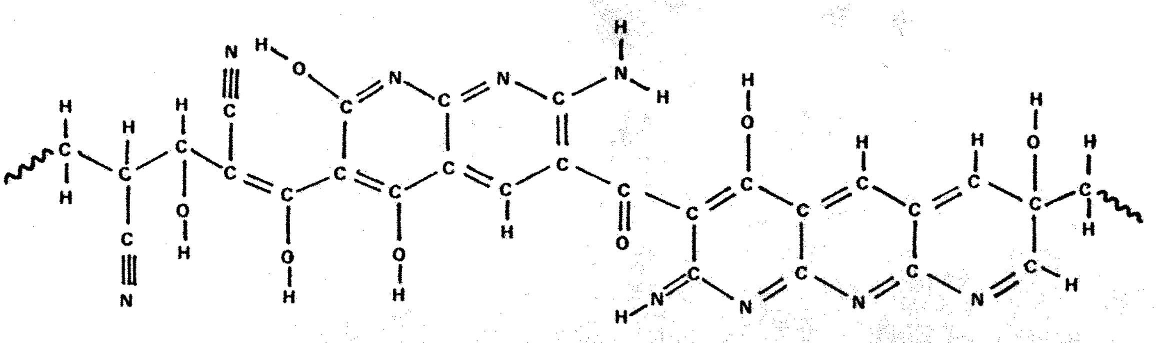

Fig. 5 A possible arrangement of the chemical groups present in partially oxidized polyacrylonitrile as indicated by infrared spectroscopy.

plus unoxidized methylene groups. Furthermore, the appearance of a strong absorption attributable to NH groups suggests that the number of rings cyclized in a sequence is small, and probably variable. These cyclized sequences will not all lie in the same plane, because the original polymer has an atactic structure, which will have a bearing on the reactions in the carbonization step. Using the basic cyclic structure proposed by Houtz[15] we have attempted to draw together these conclusions in the form of a diagram (Fig. 5) which merely indicates the type of chemical bonds which must be accounted for but which cannot be used to make structural inferences. For clarity, steric considerations including the effects of hydrogen bonding have not been included in the diagram. It seems quite likely that intermolecular hydrogen bonding is possible, the effects of which should play a role in the mechanical properties of the oxidized fibres.

When the oxidation stage is omitted from the thermal treatments, the production of high strength and modulus carbon fibres becomes more difficult and it is suspected that monomer and low molecular weight products are formed[10]. This suggests that cleavage of the linear molecules occurs, with vaporization of the low molecular weight fragments. It would then be more difficult to maintain the linear orientation of the shorter polymer molecules which remain. So the role of oxygen seems to be either prevention of the C—C bond cleavage reactions, or restraint of the linear molecules and fragments after bond cleavage, in order to maintain the orientation. Oxygen may achieve this role through some kind of bridging or intermolecular complexes, and while this work cannot comment on bridges of the type C—O—C, the involvement of hydroxyl groups appears most likely.

This work is part of a more complete study of the thermal reactions. We thank Dr B. C. Stace for his help.

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South-East Asia as a Part of Gondwanaland

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Stratigraphic evidence in Thailand and Malaya, and the fit of the South-East Asia sub-continent with India, suggest that they were once joined. It follows that, like India, South-East Asia must have drifted north to collide with mainland Asia after the break-up of Gondwanaland.

THE well known reconstructions of the ancient continents before drift by Wegener[1] and Wilson[2] showed South-East Asia as an appendage of Eurasia, as it is today. South-East Asia has not figured in reconstructions, however, either because such maps have concentrated on the southern continent of Gondwanaland of which South-East Asia was considered not to be a part[3-5], or because maps which did show the northern continent of Laurasia suffer a distortion of shape toward the edge and South-East Asia becomes unrecognizable[6], or because it lies beyond the edge of the map[7]. In his article on the palaeotectonic status of the Malay Peninsula, Burton[8] postulated that in the Palaeozoic and early Mesozoic a land-mass lay immediately to the west of the Malay Peninsula and he considered this to be India. This seems to be the only previous suggestion that South-East Asia was a part of Gondwanaland.

Whereas there is widespread agreement on the fit of Antarctica with Australia within Gondwanaland there is no generally accepted fit of Australia with India. Although most authors show the two in some way fitted together the recent reconstruction by Deitz and Holden[6] shows an oceanic embayment between them which they call the Sinus Australis. Several lines of evidence support Burton's original suggestion that South-East Asia was a part of Gondwanaland and that the most likely position of it was in the Sinus Australis, between India and Australia. It follows from this that after the break-up of Gondwanaland South-East Asia drifted northwards to collide with mainland Asia in the same way as did India.

Stratigraphic Evidence

Stratigraphic studies in Malaya[8,9] led Burton to postulate a land mass lying to the west. He supported his argument by demonstrating an approximate fit of the west side of the Malay Peninsula with the east coast of India, and by comparing the stratigraphy of the two areas. I have found in Thailand further evidence for a cratonic source of sediments to the west. A eugeosynclinal rock assemblage in South-East Thailand, near the Cambodian border, although lacking fossils, appears to be the lateral equivalent of Lower Palaeozoic, shelf-deposited argillite, cross bedded sandstone and limestone further west (Fig. 1*a*). In the Upper Palaeozoic (Fig. 1*b*) the several-kilometres thick Phuket Group with tilloid intervals passes eastwards in peninsular Thailand to a thinner, finer grained deep water facies which I interpret as a wedge of sediments, or miocline, which was laid down on the eastern flank of a land mass beneath what is at present the Indian Ocean[10]. The similarity of these tilloids, both in age and lithology, to the Talchir Boulder Beds of India is in itself suggestive of an earlier proximity of the two areas. Diamonds weathered out of the Phuket Group tilloids in Thailand could not have originated from any known ultrabasic source rock in the region and are best explained by assuming a common source with the Golconda diamond area of Andhra Pradesh, India[8,10].

In Thailand the Permian evidence is inconclusive (Fig. 1*c*) although spilitic volcanic rocks which outcrop near the Cambodian border possibly mark the northern extension of the unstable, eugeosynclinal belt of eastern Malaya; where it outcrops in the rest of southern Thailand the Permian is a shallow water shelf limestone. The Triassic of Thailand

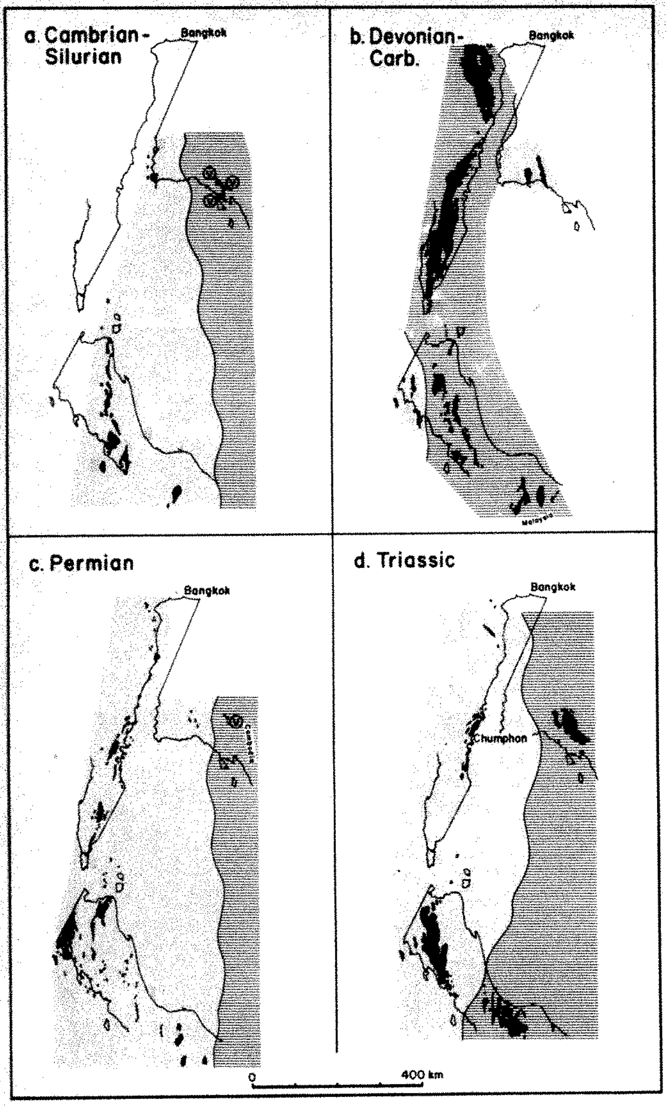

Fig. 1 Palaeozoic and early Mesozoic palaeogeography of Southern Thailand. Note that the maps are palinspastic and that the outline of the country has been restored to its shape before movement of the Khlong Marui Fault[18]. Black areas are outcrops of rocks of the ages represented by the map. Dotted pattern represents stable shelf conditions; horizontal ruled pattern represents rapidly subsiding, unstable, or geosynclinal conditions. Circled Vs are contemporaneous volcanic rocks.

(Fig. 1*d*) repeats the palaeogeography of the Lower Palaeozoic with a geosynclinal flysch belt lying to the east of shallow-water-deposited deltaic sandstones in which sedimentary structures around Chumphon show a western derivation.

An important piece of evidence on which the theory of continental drift has been built is the presence of the *Glossopteris* flora in the Permo–Carboniferous of the land-masses which comprise Gondwanaland. Permian beds near Phetchabun in north Thailand have yielded rare, fragmentary, remains of the fossils *Glossopteris* cf. *angustifolia* and *Palaeovittaria parvifolia*. Kon'no[11], who described this flora, states that these are Gondwana elements and he accounts for them in the Phetchabun flora (which also has Cathaysian floral elements) by saying that they are strays and that they migrated from Gondwanaland. A second expedition to Phetchabun led by Asama[12] failed to find any more specimens of the *Glossopteris* floral elements. Asama examined the hypotypes of the specimens collected by Kon'no and, accepting their earlier identification, he accounted for their apparently anomalous presence in Cathaysia by stating that they had evolved independently in the different continents, a process of parallel evolution. Thus both Kon'no and Asama recognized the presence of the Gondwanaland *Glossopteris* flora in South-East Asia but, instead of adopting the simpler view that this indicated that the area was indeed once a part of Gondwanaland, they devised theories of migration and parallel evolution to account for the presence of the flora. It is noteworthy that in the island of New Guinea, an undisputed former component of Gondwanaland[1-7,13], a mixed Cathaysian and Gondwana flora, also occurs[14].

Position within Gondwanaland

The fit of the west coast of the Malay Peninsula with the east coast of India which Burton[8] noted was based on the approximate fit of their coastlines; Sumatra had to be omitted because it spoiled this fit. A greatly improved fit of South-East Asia with India can be achieved if the continental edge is considered rather than the coastline (Fig. 2). For India I have adopted the 1,000 m bathymetric contour as far north as the head of the Bay of Bengal and beyond this, onshore, the line is projected so as to pass to the east of the Khasi Hills inlier which represents the easternmost known extremity of the Indian Shield. In South-East Asia, however, the position is complicated by younger Mesozoic and Tertiary fold belts which overlie oceanic crust and in places obscure the margin of the South-East Asia Shield. Thus western Burma, the Andaman and Nicobar Islands and the islands off the west coast of Sumatra have to be excluded from the reconstruction. In the Andaman Sea the edge of pre-younger Mesozoic continental crust lies just west of the base of the continental slope[15] and its northern continuation is believed to be the Shan Scarp, separating the Palaeozoic rocks of the Shan Plateau from the Tertiary rocks of the Central Belt of Burma[16,17]. Having established the extent of Palaeozoic and early Mesozoic continental crust in India and South-East Asia it is necessary to remove the effect which major transcurrent faults have had on the continental outlines. The Khlong Marui Fault[18] which crosses, and is the cause of, the prominent bend of peninsular Thailand is the largest of a group of sinistral transcurrent faults on which at least 200 km of displacement occurred in about mid-Mesozoic times. Their precise position cannot be plotted in the little explored Palaeozoic rocks of North-West Sumatra but in the Strait of Malacca unpublished seismic surveys show a number of south-trending faults between 98° and 99° east longitude. I suggest that these are the southern continuation of the fault belt mapped in Thailand. Other large transcurrent faults have been mapped in South-East Asia[19-21] but their effect on the continental outline, where known, is slight, either because displacement along the fault was not great or else because there is no evidence that the fault extends to the continental margin. The resulting fit of India and South-East Asia (Fig. 2) is remarkably close, although it does necessitate moving Ceylon to the south-west of its present position.

Fig. 2 also shows a suggested fit of South-East Asia with Australia. The margin of pre-younger Mesozoic continental crust in South-East Asia is again complicated by the younger geosynclinal deposits which have accreted onto the shield area, or else have risen along with welts of oceanic crust to form island festoons, such as most of the eastern Indonesian archipelago. The black area of overlap in Fig. 2 is younger continental area formed after the postulated break-up took place. North-west trending faults in southern Borneo[21,26,27] may mark the belt along which the original rifting away from Australia took place and they have their counterpart in western Australia in the Permian fault-belt, roughly along the 115° meridian[28] (Fig. 2).

The evidence that South-East Asia once formed a part of Gondwanaland can therefore be summed up as follows: the stratigraphic evidence is good for a former connexion with India; the palaeobotanic evidence is only moderately good because of the rarity and fragmentary nature of the all-important, alleged, *Glossopteris* flora; the fit with India is very good and with Australia good.

East and West Gondwanaland began to separate in the

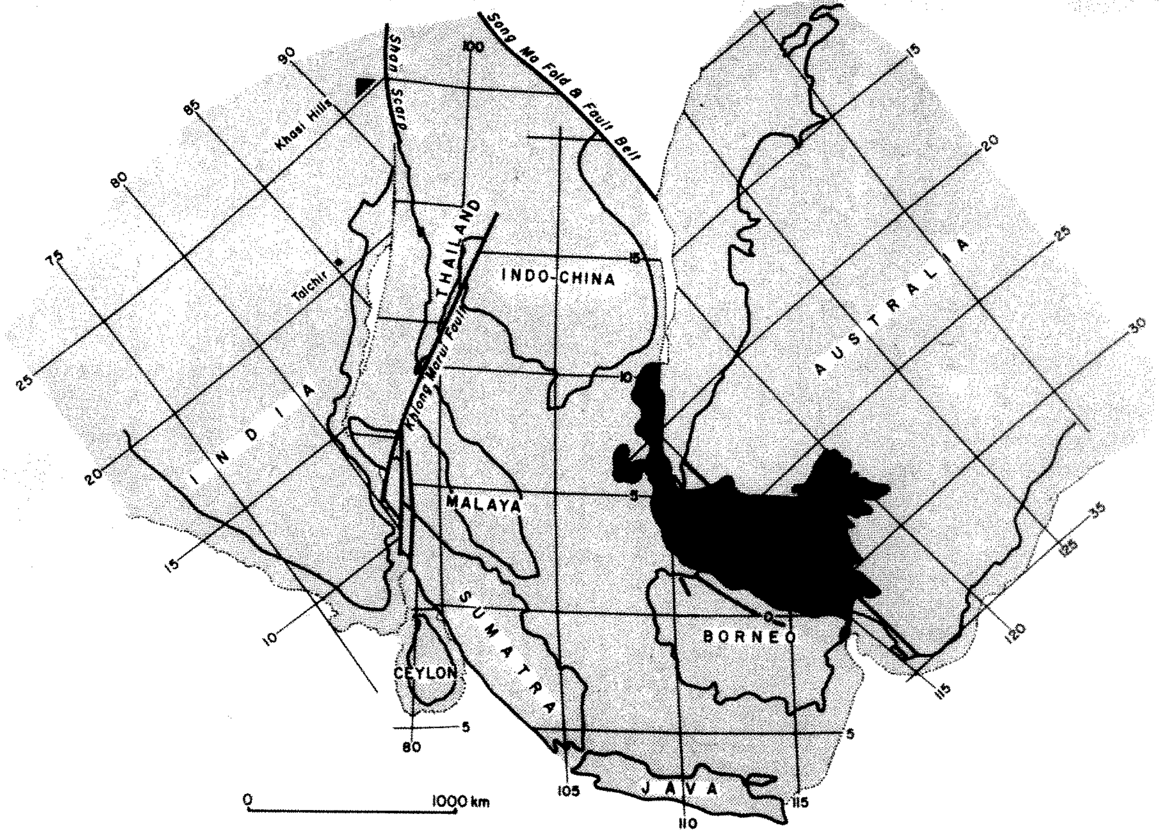

Fig. 2 Reconstruction of India, South-East Asia and Australia before break-up and continental drift. The stippled areas are bounded by the continental slope which, for India and Australia, has been taken as the 1,000 m bathymetric contour; for South-East Asia the equivalent boundary varies in depth from about 400 m on the east to 2,800 m in the Andaman Sea. Black area is overlap of Australia and South-East Asia (see text). Maps are on Bonne Projection.

Triassic according to some writers[6,22], while others[4,23] produce evidence for initial rifting in the Jurassic and Early Cretaceous. Stratigraphic indications are that South-East Asia still adjoined India in the Triassic, but separation may well have taken place in the Jurassic, at which time the sinistral transcurrent faulting of the Thailand–Malaya Peninsula was active. Whereas India and Australia retained their orientation relative to one another after break-up, it was necessary for South-East Asia to undergo an anticlockwise movement in order to attain its present orientation. Such a rotation may well have caused the numerous Mesozoic sinistral transcurrent faults which have been mapped in South-East Asia, far outnumbering those with dextral displacement (discussion meeting "Faulting in Malaysia", *Geological Society of Malaysia Newsletter*, January 22, 1970).

The line of continental collision between India and Eurasia is the Indus Suture Zone which is marked by an ophiolitic mélange belt[24]. In the past this line has been inferred to swing through a right angle at the eastern end of the Himalaya and thence to run south to the Indian Ocean. But if, as proposed in this note, South-East Asia has had a similar history to India and has collided with Eurasia, then a suture line must be present between the two. I suggest that such a line does exist and that it is the Song Ma (Black River) fault and fold belt which runs north-west from the Gulf of Tong King toward the eastern end of the Himalaya[25–27]. In this belt successive Palaeozoic and Mesozoic orogenies have taken place, although whether an Alpine Orogeny occurred, as in the Indus Suture Zone, is not certain because of the absence of rocks younger than the folded and faulted, Triassic "Middle Indosinian". Ultrabasic igneous outcrops and schistes-lustrés may be remnants of oceanic crust and continental rise sediments which once intervened between the two continents but which have now been largely subducted beneath Eurasia; possibly the upper Mesozoic and early Tertiary sediments which must have accumulated on the advancing margin of the South-East Asia continent have suffered a similar fate of subduction beneath Eurasia.

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LETTERS TO NATURE

PHYSICAL SCIENCES

On the Redshifts of Galaxies

THERE have been several investigations of possible parts in the redshifts of galaxies which are apparently not due to their radial systemic velocities[1-7]. In most of them the correlation between redshift and magnitude has been studied. To obtain more information about the nature of the possible redshift effect, other parameters should be studied. I have made a preliminary study of the redshifts of galaxies in clusters, groups and pairs in respect to type, magnitude and peculiarities of the galaxies. Systematic differences between the redshifts of different types of galaxies were found. I wish to report here some further data on the redshifts of galaxies with respect to their types, magnitudes, diameters, colours and inclinations.

Five systems of galaxies have been considered: (*a*) the Virgo cluster, (*b*) five other clusters with more than fifteen measured redshifts in each, (*c*) four distant clusters and one nearer cluster, each with two to eight measured redshifts, (*d*) thirty-five groups with three to nineteen redshifts, and (*e*) eighteen pairs of galaxies. The Virgo cluster was considered separately because it may consist of two overlapping clusters[8]. Groups and pairs were taken from I. D. Karachentsev's lists[9,10], and only systems with both spirals and SO and/or E galaxies with measured redshifts were included in the study. To avoid including the same galaxies in more than one system when all data are considered, groups and pairs which are subsystems of greater systems have been excluded. The numbers of the galaxies in (*a*)–(*e*) are 113, 175, 16, 210 and 36, respectively. The total number of galaxies studied, with known redshifts and types, is 550. The amount of data for other parameters is smaller (Table 1). Most data were taken from the reference catalogue of G. and A. de Vaucouleurs[11] and were complemented using the morphological catalogue of Vorontsov–Velyaminov, Krasnogorskaya and Arhipova[12] and an article by Zwicky and Humason[13].

So that systems with different sizes and velocity dispersions could be studied together, the dimensionless quantity $u = \Delta V/\sigma_V$ was used. $\Delta V = V_{\text{galaxy}} - V_{\text{system}}$ is the residual redshift of the galaxy (in units of velocity) and σ_V the redshift (velocity) dispersion of the system. The mean dispersions 194 km/s and 89 km/s, calculated for the SE and SSO pairs, respectively, were used for σ_V in the case of pairs. Fig. 1 gives the distributions of E, SO, S and Sbc-Sc galaxies to different u values for the five kinds of systems.

In almost all the kinds of systems, ellipticals and lenticulars show an excess of negative and spirals an excess of positive residual redshifts. Ten out of eighteen spirals belonging to mixed field pairs have positive residuals. But eight of twelve spirals in pairs which are members of larger systems have positive residuals, and thus the effect is also seen in pairs. A more accurate analysis revealed that, in particular, there was an excessive number of Sbc and Sc galaxies with positive residual redshifts. For earlier type spirals the situation is the reverse.

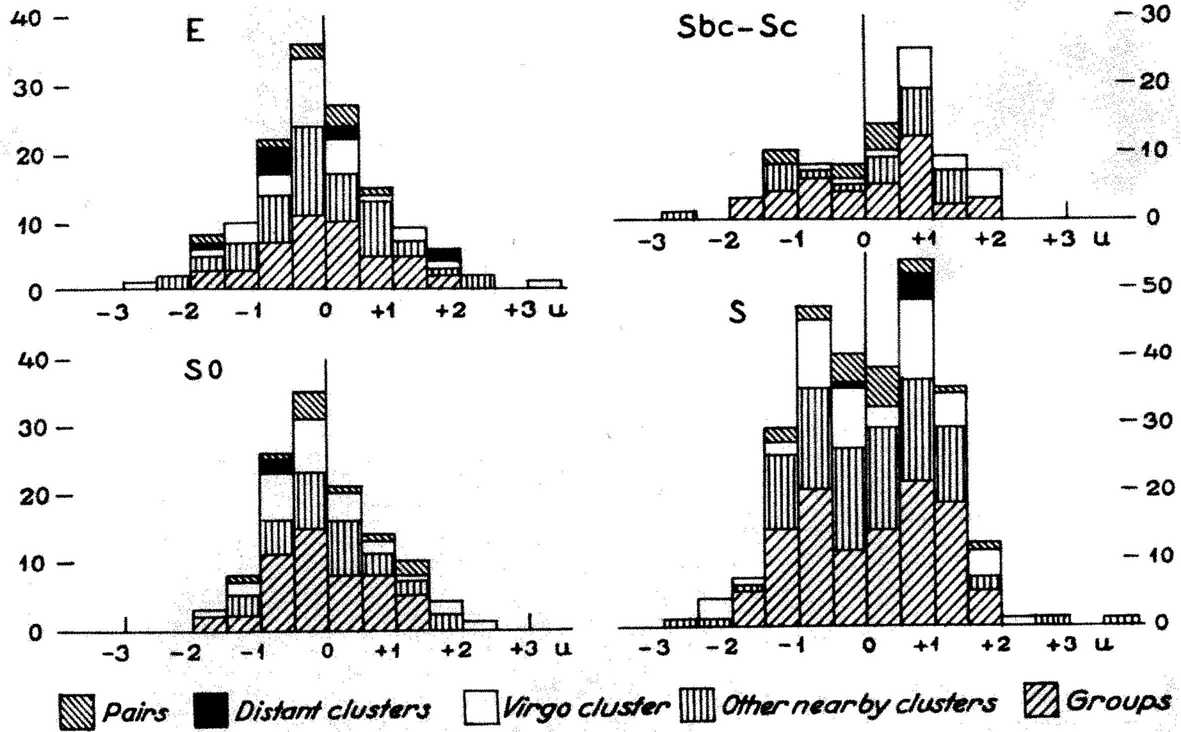

Fig. 1 Distributions of E, SO, S and Sbc-Sc galaxies to different *u* values.

The total numbers of different type galaxies n_V and the corresponding frequencies of negative residual redshifts p^- are given in Table 1, lines 1 and 2. P^- (line 3) represents the probability that a frequency appears by chance. The chance probability, that in all the five different kinds of systems a nearly similar situation is valid simultaneously, is much smaller than p^-. The next lines give the mean redshift differences $\overline{\Delta V}$, the corresponding chance probabilities $P(\overline{\Delta V})$, the redshift dispersions σ_V, the mean values of u and the dispersions of u, respectively. Field pairs are not included in the calculations.

Most of the elliptical and spiral galaxies whose types are incompletely given or not at all in the reference catalogue have relatively large positive residuals. For 16 elliptical galaxies of this kind $\overline{\Delta V} = +177$ km/s, and for 24 spirals $\overline{\Delta V} = +289$ km/s.

An analysis has been made to test the assumptions[1,5] of a systematic redshift effect depending on the magnitude of the galaxy. According to these assumptions, fainter galaxies have larger redshifts. I have calculated the linear regressions between the quantity u and the magnitude for each morphological type. This has been done separately for the absolute magnitudes M and for ΔM, the difference between M and the average absolute magnitude of the galaxies with measured redshift in the system. The parameters were normalized by dividing them by σ_M, the standard deviation of the absolute magnitudes determined for each type. The quantity b_M (line 10) is the mean of the coefficients of linear regressions calculated by these two methods. This procedure diminishes random fluctuations involved in the methods.

The problem appears to be more complicated than had been supposed. First, faint elliptical galaxies have an excess of positive residual redshifts. Six out of nine galaxies with $\Delta M > 1^m.5$ have $\Delta V > 0$ and their mean residual redshift corresponds to $+155$ km/s. (See also the third column, lines 9–11, of Table 1.) Similarly, in the case of groups of galaxies, the spirals have a weak trend in the same direction ($b_M = +0.07 \pm 0.10$ for all 102 galaxies and $\overline{\Delta V} = +194$ km/s for five faint spiral galaxies with $M > 18^m.0$). These points give some support to the assumptions made particularly by Arp[5]. Of course, part of this effect can be caused by background galaxies. Another possible explanation is that these galaxies are related to peculiar, compact galaxies and to QSOs, for which non-Doppler redshifts have been proposed.

Table 1 Mean Residual Redshifts and Coefficients of Linear Regression between the Redshifts and Various Parameters for Different Type Galaxies

Line	Quantity	E	SO	S	Sa	Sb	Sc
1	n_V	131	114	253	73	84	51
2	p^- (%)	57.3	57.9	47.4	58.9	44.0	41.2
3	P^-	0.05	0.05	0.21	0.06	0.14	0.11
4	$\overline{\Delta V}$ (km/s)	−39	−28	+30	−124	+56	+131
5	$P(\overline{\Delta V})$	0.20	0.28	0.18	0.02	0.17	0.04
6	σ_V (km/s)	645	433	487	463	406	517
7	$\bar{u}$	−0.07	−0.05	+0.06	−0.18	+0.13	+0.20
8	σ_u	0.98	0.80	1.01	0.95	0.96	1.16
9	n_M	120	109	242	70	83	51
10	b_M	+0.09	+0.02	−0.01	+0.09	−0.12	−0.02
11	D_M	±0.10	±0.07	±0.06	±0.11	±0.11	±0.15
12	n_M (clust)	75	59	139	39	40	30
13	b_M (clust)	+0.11	−0.02	−0.07	+0.19	−0.24	−0.30
14	D_M (clust)	±0.12	±0.11	±0.09	±0.15	±0.16	±0.22
15	n_D	121	109	243	68	84	51
16	b_D	−0.05	−0.02	+0.02	−0.15	+0.11	+0.10
17	D_D	±0.09	±0.08	±0.07	±0.12	±0.11	±0.16
18	n_{C_0}	65	75	153	44	58	31
19	b_{C_0}	−0.09	+0.05	−0.10	−0.06	−0.05	−0.36
20	D_{C_0}	±0.12	±0.10	±0.08	±0.15	±0.13	±0.18
21	$n_{\log R}$	121	109	243	68	84	51
22	$b_{\log R}$	−0.04	+0.08	−0.14	−0.21	−0.13	−0.18
23	$D_{\log R}$	±0.09	±0.08	±0.06	±0.12	±0.10	±0.17

The second point of the redshift-magnitude problem is that Sb and Sc galaxies in clusters seem to behave conversely to that discussed above. As can be seen from the lines 12–14, bright late-type spirals have the largest positive residual redshifts. If real, this kind of effect cannot be explained by means of foreground or background galaxies. It follows that there is no such redshift effect, in the direction assumed previously[1,5], which could have influence within the whole magnitude region.

When galaxies with negative velocities are excluded, the spirals in the Virgo cluster have $b_M = -0.08 \pm 0.14$. This is against the assumption that the Virgo cluster could be a superimposition of two separate clusters.

The principal results for the other physical parameters are given in the lines 15–23. The parameters in question are shown as subscripts. D means the linear diameter (Hubble constant $H = 75$ km/s/Mpc), C_0 the colour index, log R the logarithm of the ratio of major and minor axes of the galaxy. The regression coefficients have been calculated by a method similar to that used for the magnitudes.

As expected, because of the mutual dependence between magnitude and diameter, the coefficients of regression for D roughly follow those for M with opposite sign. The lines of regression for C_0 are in most cases in the direction which is expected when the redshift differences and the colour variation are taken into account. This suggests a continuous change of the amount of the additional redshift as a function of type and thus gives a further proof of the reality of the redshift effect.

If the redshift effect is connected to physical conditions in the nucleus of the galaxy, one might not be able to observe it in very inclined galaxies. Indeed, according to lines 21–23 of Table 1 this seems to be the case. Most galaxies with known rotation curves have quite large inclinations. Possibly for this reason distinct redshift differences between the nucleus and other parts of the galaxy have not been observed. These differences would be expected if the effect were due to the nucleus.

It is shown that E, SO and Sa galaxies have excessive negative and Sb and Sc ones excessive positive residual redshifts. At the same time, for the latter there are several statistically significant correlations between the redshift and other parameters. The result means that in some part even for normal galaxies, of late Hubble types, with small colour indices and small inclinations, part of the redshift cannot be explained by systematic velocity. Because the average redshifts have been considered here, the explanation proposed by Lewis[6], that outward gas motion from nuclei of central galaxies would be the reason for systematic differences in redshifts, is not valid.

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Westward Displacement of the Lithosphere

THE peak of the oceanic and solid Earth tidal bulges lead the overhead position of the Moon and the couple is[1]

$$-N=\frac{8}{5}\pi G M \rho_1^4 u_r\, d \sin 2\varepsilon \qquad (1)$$

where G is the Newtonian constant, M the Moon's mass, ρ_1, the radius of the Earth body, c, the distance between centres, u_r, the radial displacement, d, the density of the matter in the bulge and ε, the phase displacement (Fig. 1). The sum of the couples is known to be between 3.9 and 5.3×10^{23} dyne cm from observations of the acceleration of the Moon in orbit and the reduction of the Earth's rotation rate[2].

The contribution from the oceanic inequilibrium bulge is, however, not known precisely[3]. But it can be shown that most of the retarding torque is engendered in the outer part of the Earth.

The couple acting on the part of the Earth from 400 km downward is 6.61×10^{20} dyne cm if a value of Q of 800 is taken for the lower mantle and a liquid core having small mantle coupling; this value is suggested by the work of Lagus and Anderson[4]. Subtraction of this couple from the astronomically observed total suggests that a torque of not less than 3.8×10^{23} dyne cm tends to displace the lithosphere westwards about the mantle below it—both the couple arising in shallow seas and that in the upper mantle contribute to the torque at the bottom of the lithosphere. In effect the couple on the oceans and the lithosphere is responsible for most of the terrestrial deceleration. It is hard to believe that such a force acting for geological times on an Earth suffering differentiation has not caused displacement. We do not know precisely, however, the value of the viscosity in the low-velocity zone which opposes the couple (Fig. 2).

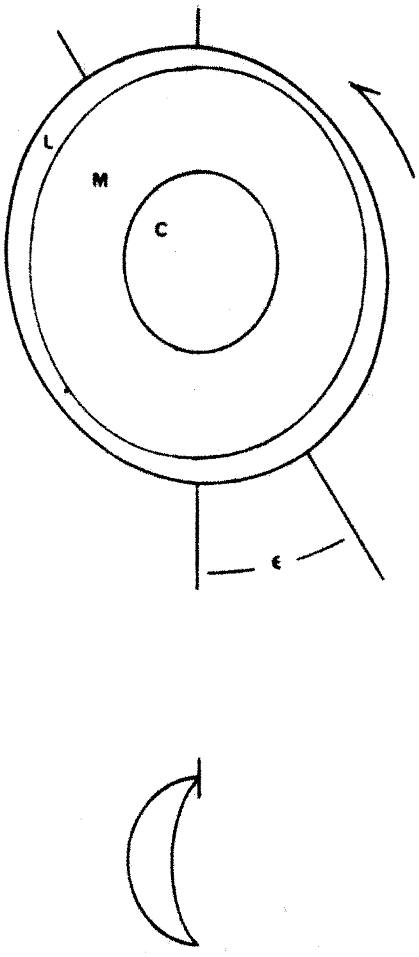

Fig. 1 Relationship of the phase lead in the tidal bulge, ε, with reference to the overhead position of the Moon in respect to L, the lithosphere and low velocity zone; M, the lower mantle; and C, the Earth's core. ε is related to Q, the propagation quality factor of seismic waves, in such a fashion that $Q^{-1} = \tan \varepsilon$. If now a set of values of Q, as determined by Lagus and Anderson[4], is chosen so that Q in the mantle below 400 km is 800, and the liquid core nearly maintains phase equilibrium position (see also Malkus[5]), the phase lead of the bulge in M is some 4′ of arc and the couple acting on this shell is 7.8×10^{20} dyne cm (equation (1); u_r has been determined by Takeuchi[22]). All high-Q mantle values lead to similar results. But the total torque is known from astronomical observations to be in excess of 3×10^{23} dyne cm; thus almost all the retarding torque is engendered in L, which is responsible for diminishment in rotation of M by drag exerted at the top.

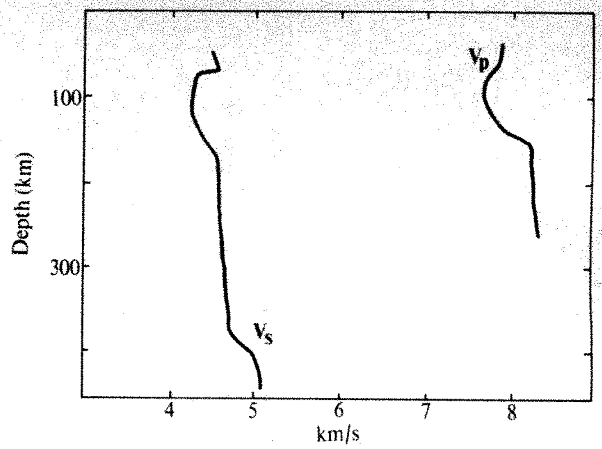

Fig. 2 A representation of the drop in seismic velocities at the base of the Earth's lithosphere, from Anderson and Sammis[6], who conclude that the sharpness of the drop must represent a condition of partial melting. The relationship between the velocity decline, Q the propagation quality factor, and the viscosity is not precisely known, but it appears certain that the viscosity decline is also abrupt and of considerable amplitude.

Although most of the lithosphere is about 70 km thick[6], its thickness does vary regionally to some two or three times this figure. If the lithosphere were known to be suffering displacement and if some regions offer greater resistance than average to being displaced, then effects to be expected include the westerly rotation of the lithosphere about the poles and the breakup of the lithosphere into segments because the resistance to rotation is not regionally uniform; these segments should themselves tend to rotate while suffering westward translation. The plates should break up and reform through time, as their orientation relative to the couple and the resistance forces changes, and the plate rotation should most frequently be clockwise in the northern hemisphere and counterclockwise in the southern hemisphere. Plates encountering resistance should be displaced more slowly and so some plates will tend to override or underride the plate to the west; elsewhere the junction will be extensional.

Compression and extension will also be principally aligned east–west and the world rift system should align itself predominantly north–south at low latitudes The rate of rifting should be maximum in low latitudes, at high latitudes there should be a tendency for it to swing east–west. Westward drift will not be apparent to us; but it will appear that surface features related to the underlying mantle, for example persistent volcanic rock sources, have a tendency to migrate east.

The displacement of lithospheric segments by tidal drag might act either independently or in conjunction with thermal convection and must ultimately result in an equilibrium situation. The displacement of a lithosphere consisting of irregular plates must lead to changes in the location of the principal moments of inertia and hence to drifting of the rotational pole.

Several of these criteria are exhibited by the real Earth. Verhoogen *et al.*[7] have drawn attention to the polar aspect of the great surface features and Morgan[8], Le Pichon[9], and McKenzie[10], among others, have described the rotation of the lithosphere plates. Regional strength variations in the lithosphere must lead to departures in the resultant strain but over periods of time these should average out. Fig. 3 is Le Pichon's representation of surface-feature displacement in the past 10 m.y., in effect the vector sum of the displacement suffered by the segments comprising the lithosphere. Equatorial displacement has been 500 km to the west relative to a polar land mass and displacement evidently dies out towards the poles. The eastward decrease in age of Hawaiian and other such volcanic centres is consistent with a migration of volcanic sources in the underlying mantle and reconstructions of the continents using palaeo-pole magnetic evidence suggest not only that rotation was counterclockwise in the southern hemisphere but that displacement of the lithosphere was accompanied by displacement of the pole[11]. Contemporary lithospheric displacement is more difficult to detect from relatively short seismic records. It might be suspected at most that Earth tide peaks have a triggering effect for earthquakes, but the period of the high frequency Earth tides is shorter than the relaxation time of even the less viscous parts of the mantle. Statistical decomposition of the incidence of earthquakes in terms of Earth tidal peaks has shown[12,13] that no correlation exists.

The forces set up by tidal drag have an important residual effect—the tangential strain imposed at a point in the low velocity layer by one rotation of the Earth is added to the displacement, however small, remaining from the previous day's shear. The most plausible model of the viscosity distribution in the Earth's outer layers, a hard shell overlying a soft one, will distribute strain so that it accumulates in the low velocity zone.

Most seismic energy is released at the time of large shocks and the strain field present in the focal region of large earthquakes is coherent over large regions of the surface[14]; this strain seems representative of the primary tectonic mechanism (whatever this may be). Analyses of the incidence of large earthquakes with respect to astronomical conjunctions have been made by Tamrazyan[15].

Table 1 * Incidence of Earthquakes $M=7.9$ to 8.7 during the Synodic Month occurring within 2.5 Day of Lunar Perigee, for Interval 1903 to 1956

	No. of earthquakes during			Energy in units of 10^{23} erg during			Energy in % unit time	
M	Quadrature	Syzygy	Total	Quadrature	Syzygy	Total	Quadrature	Syzygy
8.7		1	1		70.8	70.8	100	982
8.6		1	1		50.1	50.1		
8.4	1	5	6	25.1	125.6	150.7		
8.3	1	5	6	17.8	89.0	106.8	100	267
8.1	3	2	5	26.7	17.8	44.5		
7.9	2	8	10	9.0	36.0	45.0		
Total	7	22	29	78.6	389.3	467.9	100	495

* Abstracted from Tamrazyan[15].

Large earthquakes are most common at the time of syzygy (Table 1) and this enhancement is accentuated at the time of lunar perigee, so that seisms are most common at the time when the Earth is close to the Moon and both are in line with the Sun. Most large earthquakes occur after the epicentral region has passed the sublunar or subsolar point and the effect is enhanced at the time of passage of major geoidal highs.

It is difficult to correlate these coincidental occurrences with Earth tide forces, partly because these vary much less with lunar perigee than with time of day and because they are symmetrical about the zenith position of the Sun and Moon. Tidal attraction varies as the cube of the distance to the disturbing body but the couple varies as the sixth power; for similar reasons the enhancement in couple at syzygy is greater than the enhancement in tidal attraction. The phase lag in the incidence of large earthquakes with respect to the overhead position of the Sun and Moon is coincident with the imposition of horizontal force in such a direction and sense as to increase accumulated shear strain if this is due to the solunar torque. The incidence is out of phase with either the maximum or minimum of tidal attraction. A build-up of stress followed by rapid displacement of material in a latitudinal direction associated with an earthquake would fit the excitation and decay of the Chandler wobble as depicted by Mansinha and Smylie[16] and by Myerson[17].

The release of seismic energy is about 10^{26} erg yr^{-1} and the angular energy of the Earth annually dissipated in the oceanic

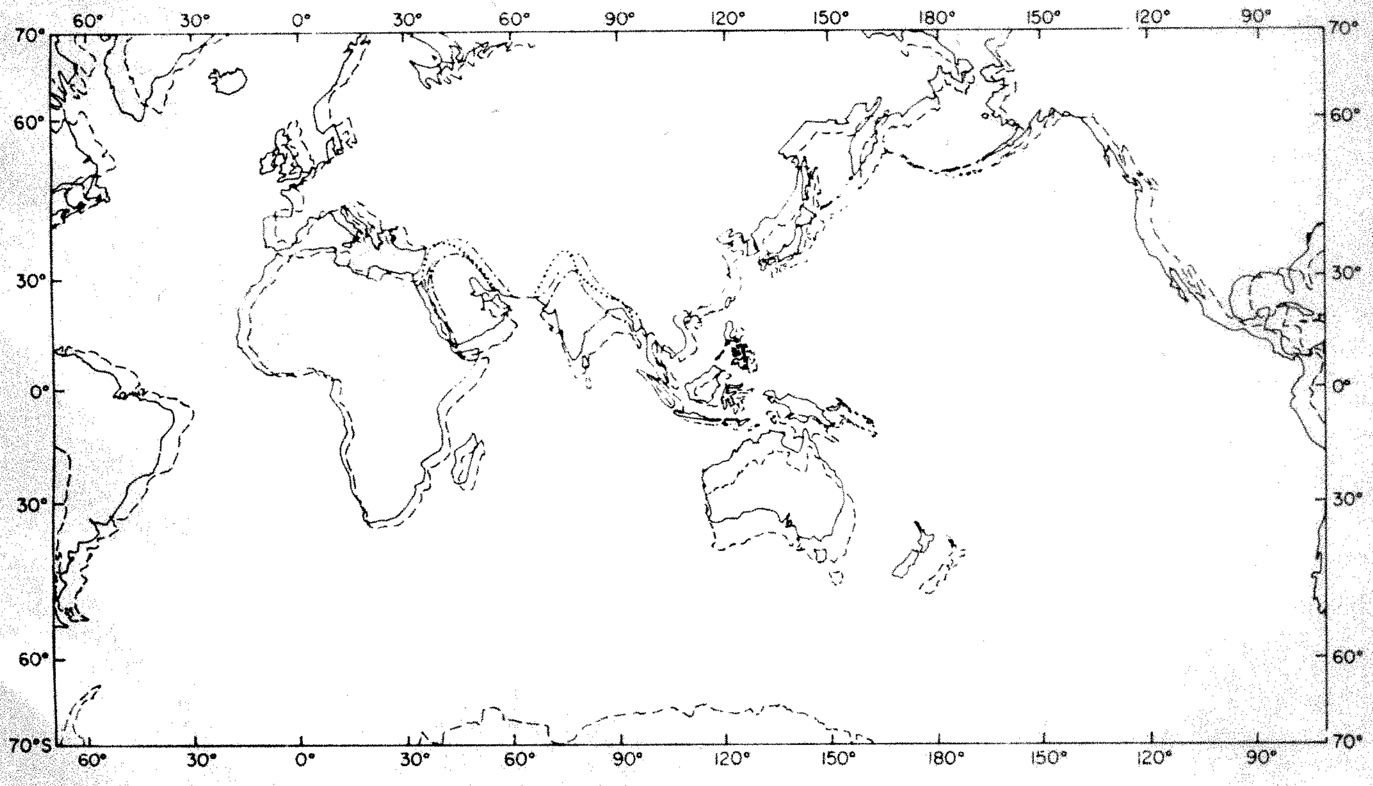

Fig. 3 Present (solid line) and past position of continents, based upon palaeomagnetic evidence[9].

and solid-earth tides is between 4.4 and 13.3×10^{26} erg[2,4]. Jeffreys[18] has concluded that most may be attributed to marine dissipation but contemporary information[6,19] suggests that much energy loss is by dissipation within the mantle, so that even in the absence of thermal convection, the solunar couple is adequate both to displace the lithosphere and to cause earthquakes. The strength of layers within the low-velocity zone and their thickness can simultaneously be made extremely small without contravening observations of Q, dispersion, or the tidal energy dissipation[20] (Fig. 2). All seismicity is strongly latitude dependent[21].

A model of contemporary tectonism, based on variable resistance of the mantle to a lithosphere suffering westerly displacement, would require that the segment most rapidly displaced west is the Pacific and that the Pacific plate is therefore impinging on the Asian, resulting in the West Pacific belt of tectonism. The North American plate must be left behind by the Pacific plate, leading to extension, greatest at equatorial latitudes, along the East Pacific Rise. The South American–South Atlantic plate must gain on the plate lying west of South America which continent thus overrides the seafloor and the European and African plates must drift west more slowly than the American plates.

Superimposed on the drift is rotation of individual plates in response to the latitudinally varying couple and mantle reaction. If the past 10 m.y. is typical (Fig. 3) the lithosphere moves west at 0.014 cm day^{-1} in the equatorial zone. This represents a rotation rate of the lithosphere relative to the mantle of 7.8×10^{-9} radian yr^{-1}. The displacement varies regionally in accordance with the resistance to its movement and because the couple itself varies regionally as the shape of the geoid.

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Vaporization Waves in Explosive Volcanism

THE necessary conditions for explosive volcanism cannot yet be stated, but certain tentative requirements emerge from the study of pyroclastic rocks and from the observation of erupted magmas. In the first quantitative report on the mechanics of ash formation, Verhoogen[1] required that the magma have high viscosity and a large gas content. More recently McBirney and Murase[2] emphasized that the disruptive force of gas pressure must exceed the combined surface tension and tensile strength of the liquid. Both articles describe the vesiculation of a magma in terms of the formation, motion and coalescence of bubbles. I wish to point out a novel fluid dynamic process which may control the production of ash and pyroclastic material emanating from a major eruption of the Plinian type.

In considering how prototype explosive volcanism can be visualized I take one dimensional shock tube flow as an analogue. In a shock tube after the diaphragm is punctured, the compressed gas expands like a piston, a shock wave develops and races ahead of the contact surface between driver and driven gas, and an expansion wave, or "relief wave", proceeds backward into the reservoir of stationary compressed gas[3]. Observe that the shock and the expansion travel in opposite directions, and the head of the expansion wave moves with the speed of sound into the compressed driver gas.

I shall consider prototype explosive volcanism to commence with the disruption of a magma chamber roof, the expulsion of a plug or the sudden opening of a fissure. Any of these will be assumed to expose high temperature magma to low pressure ambient atmosphere. My interest centres on what happens when the expansion wave reaches the exposed magma surface. This surface, the principal contact surface of the flow, commences to press against the ambient atmosphere like a piston. In so doing, each fluid particle expands toward larger specific volume. If the thermodynamic path of the expansion extends into the two-phase field, partial vaporization must result. The head of the wave travels back into the unexpanded fluid at the vaporization speed of sound for the fluid at its particular state point in the coexistence region. This speed is determined by the slope of the adiabat in the two phase region or on its liquidus boundary. The vigour of the expansion depends on the excess of vapour pressure over the ambient atmospheric pressure. Its speed depends on the derivative of vapour pressure with absolute temperature, and is about an order of magnitude smaller than the sound speed in the liquid.

Because the magma is a poor conductor and its specific energy is limited, the expansion will be essentially adiabatic and will in general only partially vaporize the fluid. After the magma partially vaporizes like a uniform fluid, we must visualize a situation of extreme complexity in the real case where blobs and droplets of expanded, molten, vesiculating magma are carried aloft with an expanding vapour which rapidly cools and from which condense steam, pumice and other particles. The whole mass, now at reduced density, moves with local velocities of flow depending on particle position in the expansion wave. As the flow expands in a solid angle sector it does work against the surrounding atmosphere and consequently slows down. Gravitational and thermal convection effects dominate the ensuing motions.

I have earlier discussed the expansion of a compressed, uniform fluid with high enough specific energy so that an appreciable fraction can vaporize[4]. The aim was to provide a model for the expansion of superheated metals as encountered in experiments with exploding wires, but the results are of general application. In the case of metals the expansion of dense fluid behind the contact surface takes place with the production both of high temperature vapour and expanded liquid matter in an alternating configuration called "striations". X-ray shadow graphs obtained for a number of metals[5] show that the striations occur during the passage of the vaporization wave. The simplest explanation of their presence connects them directly with the vaporization process as evidence of the manner in which a fluid of uniform density partially vaporizes.

In a magma the form and separation of striations may be quite different from those found in metals, but the essential process of vaporization, without apparent nucleation and bubble formation, may be the same. The dispersion of denser matter in elongate filaments or sheets, with a somewhat random distribution of small deviations from parallelism, seems to provide a physically realized alternative to bubble formation. The time scales are clearly separated by several orders of magnitude. The microscopic processes remain to be worked out.

While the expanded material will be less dense than magma, it will nevertheless still be heavy and hot with respect to the ambient atmosphere. It is this matter which comprises the *nuées ardentes* flow. In observing the eruption of Lopevi volcano, Warden[6] reports that a heavier portion of the ash cloud welled up above the crater rim and flowed down the western side of the cone. Heavier ash and lapilli fell out before portions of the cloud started to rise convectively. Pulsations of ejected molten lava vesiculated and disintegrated passing immediately into the grey ash cloud. Moore and Melson[7] exhibit a number of pictures taken at Mayon in the Philippines of *nuées ardentes* following a puff of glowing lava which rises above the crater rim for hundreds of metres. These downfalls of hot, dense material are evidence of expanded magma returning to Earth in the gravitational field. From the fluid dynamical theory just outlined we now understand the glowing clouds of violent volcanism as one consequence of the vaporization expansion behind the magma contact surface.

In the investigation of vaporization waves in metals we have developed a thermodynamic model to represent the presumed situation[8,9]. Because of the lack of high temperature data for metals, and for nearly all substances, one cannot calculate the sound speed with which the expansion wave propagates using measured values. In order to proceed I assume that a modified version of the van der Waals equation can be used as an equation of state with its constants determined from recent estimates of pressure, temperature and specific volume at the critical point. The modification consists in relinquishing the Maxwell equal-area rule for determining the horizontal isotherms in the two-phase region. Kahl has shown[10] that a generalization of this requirement allows the specific heat at constant volume for the liquid and vapour phases to be chosen separately as integrable functions of temperature. I further assume that the expansion takes place along the liquidus boundary of the two-phase region under conditions of local thermodynamic equilibrium. Sound speed values calculated from this model compare quite well with measured values of expansion wave speed for several metals in giving the specific energy of onset of the wave and the form and magnitude of the wave speed function. At higher temperatures various deviations are present and some hypotheses have been offered to explain these discrepancies. Our knowledge of the details of the expansion fluid dynamics and of the connexion between density and conductivity of the metal is still in a rudimentary stage.

To carry these ideas over to the problem of expansion of magma, one has to assume that during the early part of the expansion the complex molten mixtures obey an equation of state similar to the van der Waals. The evidence for metals suggests that for a wave-speed limited expansion to occur the liquid must be at some temperature like 2/5 critical or higher. Otherwise the wave speed may be so near to zero that other processes such as nucleation and bubble formation predominate. Because observed magma temperatures do not exceed roughly 1,700 K, the question arises whether any magma mixtures, particularly those rich in water, have critical temperatures as low as 4,200 K.

How the critical temperatures of uniform mixtures of compounds will vary with water content is unknown. If the rate at which small additional amounts of water will depress the two-phase critical temperature is very steep for water contents less than 10% by weight, we may expect non-zero vaporization wave speed at magma temperatures.

The existing knowledge of critical temperatures of liquid mixtures is confined at present to pairs of permanent gases and some organic liquids. Similarly, the theoretical calculation of state equations for binary mixtures is limited to the study of the van der Waals theories of hard sphere mixtures, or average potential model and perturbation theories based on some empirical data and the law of corresponding states. Thus, while it is possible that some theoretical calculations for mixtures of idealized magma components might be attempted, the approximations would be severe and, at present, there are no experimental data with which to compare. Perhaps a more rewarding approach is to attempt experimental production of shock-tube like flows of high temperature magmatic mixtures tempered with varying amounts of water. Optical, electrical and X-ray techniques used in the recent studies of expanding metals should prove to be adaptable to the problems of laboratory simulation of explosive volcanism.

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Temperature Changes associated with Adiabatic Decompression in Geological Processes

WALDBAUM[1] in a recent thought-provoking article is the first, I believe, to direct geologists' attention to the Joule-Thomson coefficients of minerals as potential heating agents in the Earth. It is unfortunate that he overlooks the change of gravity potential of vertically moving masses because this omission invalidates his more interesting conclusions.

The chief reason for the decompression and the thereby connected isenthalpic temperature rise assumed by Waldbaum is the ascent of masses through the Earth's mantle and crust (Fig. 1 in Waldbaum's article). It is, however, easy to show that the increase of gravity potential during the ascent compensates for a major part of the decompression, thus making the heating even in ideal conditions (for example, complete thermal insulation) always less—and usually much less—than given by the Joule-Thomson coefficients as quoted by Waldbaum.

The Joule-Thomson coefficient is ordinarily defined by the expression used by Waldbaum:

$$\left(\frac{\mathrm{d}T}{\mathrm{d}P}\right)_H = \frac{(T\alpha-1)V}{C_p} \qquad (1)$$

where T is temperature, P pressure, V specific volume, C_p heat capacity at constant pressure and α thermal expansion at constant pressure. The index H indicates isenthalpic conditions. Because α is very small for minerals and magmas their Joule-Thomson coefficients are usually negative so that a rise of temperature follows from a fall in pressure.

The difficulty arises from the fact that equation (1) does not include the effects of gravity but is developed for systems in which pressure and temperature are the only variables, as is usually assumed in books on chemical thermodynamics. It is derived from the enthalpy equation:

$$dH = C_p\, dT + (1 - \alpha T) V dP \qquad (2)$$

which for isenthalpic processes is simply equated to zero[2]. For systems displaced vertically in a gravitational field the enthalpy is constant only if the gravity potential is incorporated in the enthalpy expression which accordingly may be written:

$$dH = C_p\, dT + (1 - \alpha T) V dP + V \rho g dh \qquad (3)$$

where p is density, h height in a gravitational field the acceleration g of which is assumed constant for convenience. Hence for vertical movement in the gravitational field isenthalpic condition $dH = 0$ yields a modified expression for the Joule-Thomson coefficient:

$$\left(\frac{dT}{dP}\right)_H = \frac{\left(T\alpha - \frac{\rho g dh}{dP} - 1\right) V}{C_p}, \text{ or} \qquad (4)$$

because $\rho g dh = -dP^*$ where P^* is pressure at hydrostatic equilibrium,

$$\left(\frac{dT}{dP}\right)_H = \frac{(T\alpha + dP^*/dP - 1) V}{C_p} \qquad (5)$$

The conclusions which follow are valid even if we use the ordinary definition of enthalpy as a quantity independent of the gravity potential, that is, $H = U + PV$ rather than $H = U + PV + \rho g h V$ from which equation (3) derives. When the ordinary definition of H is employed, however, the condition

$$dH + \rho g dh = 0 = C_p dT + (1 - \alpha T) V dP + V \rho g dh$$

rather than $dH = 0$ must be used if the energetics of the vertical component of flow is to be compared with isenthalpic flow component in the horizontal direction.

Under ordinary vertical flow in the Earth the true pressure is not very different from the hydrostatic pressure, otherwise the movements of plastic rocks and magmas would have been faster than we have reason to believe they actually are; that is, dP^*/dP is positive and close to unity. It follows that the negative Joule-Thomson coefficients applicable to vertical motion are generally much smaller numerically than those used by Waldbaum. Only when $dP^*/dP \to 0$ does the Joule-Thomson coefficient for ascending flow approach the value given by the conventional expression (1). But to make dP^*/dP approach zero the density must either be exceptionally small and/or the vertical pressure gradient exceptionally large. A very narrow constriction in a magma-conveying fissure may possibly do the trick.

It is interesting that for descending flow equations (4) and (5) show that the heating may be even larger—at least theoretically—than indicated by the conventional Joule-Thomson coefficients. This happens when $dP^*/dP < 0$, that is, when the true pressure in the medium increases upward. This admittedly unlikely situation leads if, and when, it happens to a strong downward flow and a particularly large rise of temperature on the low pressure side.

Another noteworthy deduction follows from equation (4) by inserting the condition for constant true pressure throughout the system, $dP = 0$. This gives

$$\left(\frac{dT}{dh}\right)_H = -\frac{\rho g}{C_p} \qquad (6)$$

Constant pressure throughout the system also means descending flow (because, of course, the driving pressure gradient for vertical motion is not dP/dh but $dP/dh - \rho g$), and equation (6) simply states that the vertical temperature gradient thereby produced corresponds to a complete dissipation of potential gravitational energy to thermal energy: $\rho g dh = -C_p dT$. This is reasonable because there is no decompression or compression when the material moves downward under constant pressure.

The condition $dP = -\rho g dh$ which corresponds to hydrostatic equilibrium is also interesting to consider. This condition changes equation (4) to a form valid only for hydrostatic equilibrium:

$$\left(\frac{dT}{dh}\right)_H = -\frac{T\alpha g}{C_p} \qquad (7)$$

which is the expression for the so called adiabatic gradient.

Now, when $dP = -\rho g dh$ gravitational stability exists and spontaneous vertical motion does not occur. Nevertheless we may imagine that a thermally insulated portion of the fluid is moved up or down by an auxiliary force while the condition $dP = -\rho g dh$ is maintained. The adiabatic cooling affecting an elevated portion of the fluid and the adiabatic heating affecting a subsided portion are then given by equation (7).

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Fossil Tracks in the Meteorite Angra dos Reis: a Predominantly Fission Origin

INVESTIGATIONS of recordable lengths (maximum etchable lengths) of fossil tracks in meteorites and in lunar samples have provided information on the charge composition of cosmic ray iron group and heavier nuclei[1-3] and on the spontaneous fission contributions since the solidification of these extraterrestrial samples[4-6]. The concentration of uranium (and also transuranic elements) is usually very small (0.01–10 p.p.b. by weight[4,5]) in the silicate crystals where the fossil tracks are studied, so most of the tracks are due to cosmic ray nuclei[6]. We have studied a few meteorites having relatively high uranium concentrations for fossil tracks as well as for neutron induced tracks in previously annealed samples. In particular we studied the meteorite Angra dos Reis (ADR), an augite achondrite, which is known to have a high uranium concentration (> 170 p.p.b. by weight)[7-9] and for which the concentrations[10-12] of rare gases, both fissiogenic and cosmogenic, are well known. ADR is rich in pyroxene (the only accessory mineral present is olivine[13]) occurring as dark brown but fairly large thin transparent crystals having dimensions of 300–500 µm.

The normal etching time for revealing well formed tracks was 40–45 min in a solution of 60% sodium hydroxide by weight at its boiling point[2]. For revealing TINT (track-in-track) and TINCLE (track-in-cleavage) types of confined tracks, having both their tips within the crystal[2,6], the etching times were up to three times that for normal etching. The number densities of tracks intersecting a polished surface, henceforth called areal track densities, were counted after etching for about 60 min. The measurements of lengths of confined tracks were made after decorating track holes with silver. Details of the techniques used are given elsewhere[3,5,6].

Fig. 1 shows photomicrographs of fossil surface tracks, that is those which appear on etching a polished surface, and also of TINTs and TINCLEs in ADR. Fig. 2*a*, *b* and *c* shows tracks measured in a systematic scan in which all confined tracks having a dip angle (with respect to vertical) of ≥ 60° were measured[5]. As a result of measurement of well developed and thin tracks and remeasurements after an additional etching, we have established that the track length measurements

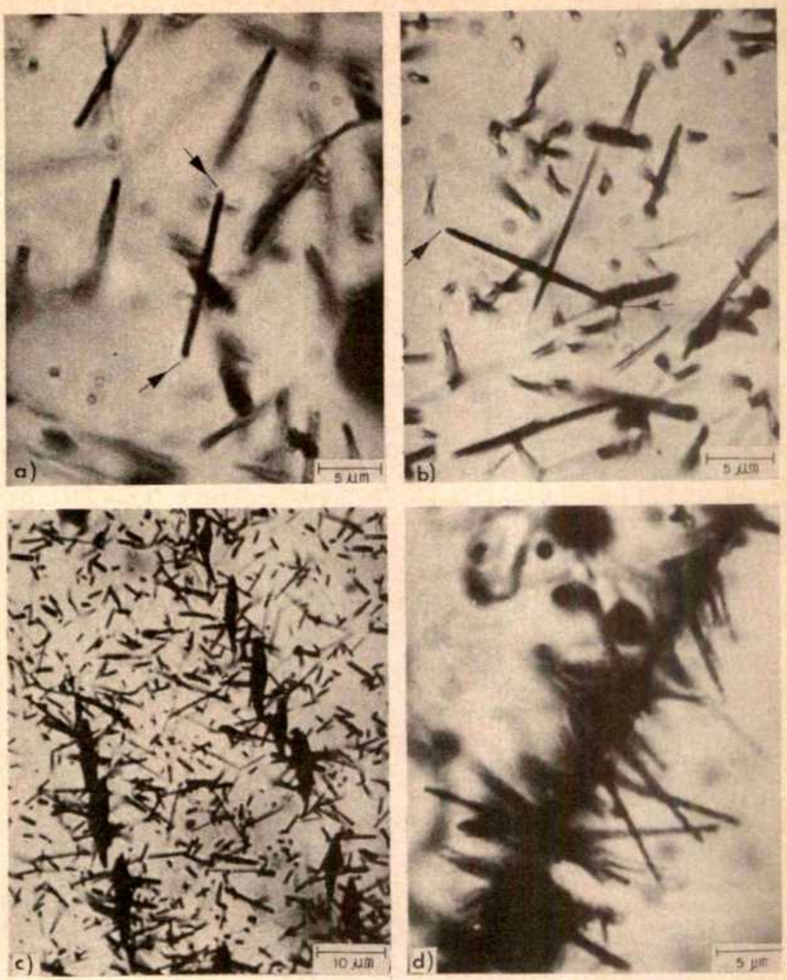

Fig. 1 TINTs (*a*, *b*), surface tracks (*c*), and TINCLEs (*d*), in the meteorite, Angra dos Reis. In *a* and *b* TINT tips are shown by arrows. All the tracks are silvered.

correspond to the maximum etchable lengths of tracks within about 0.5 μm (MacDougall *et al.*, unpublished results).

To understand the observed length distribution of fossil tracks in ADR, ADR and other meteorites, Kapoeta, Moore County and so on, were annealed and irradiated by a flux of thermal neutrons (nvt $= 5\times10^{16} - 5\times10^{18}$ cm^{-2}). The results of measurements of lengths of neutron induced tracks in ADR are shown in Fig. 2*d*, *e* and *f*.

The distribution of areal densities (cm^{-2}) of fossil surface tracks, based on 5,000 tracks in 47 crystals, is shown in Fig. 3*a*. The weighted mean fossil track density is computed to be 1.2×10^{7} cm^{-2}. The distribution of areal densities in the case of neutron induced fission tracks is shown in Fig. 3*b*, for a sample of 34 crystals.

We infer from Fig. 2 that the distribution in the recordable lengths of tracks based on TINTs or TINCLEs is similar for tracks from both fossils and neutron induced fission, both having a value of 14.3 ± 1 μm.

The observed length distribution of fossil tracks in ADR (Fig. 2) is unique, being unlike any other meteorite[2,5] or lunar rocks and dust, inasmuch as the tracks shorter than 15 μm (due to cosmic rays) are rare in ADR. Stopping[1–3] cosmic ray nuclei gives tracks of up to several hundred microns; a majority of the tracks, identified with the abundant iron group nuclei, however, have short lengths, <15 μm. It has been inferred from a systematic analysis that nuclei of vanadium, chromium, manganese, iron and cobalt respectively lead to tracks of etchable/recordable lengths of 2.5, 5.5, 8.5, 11.5 and 15 μm in pyroxene[2,5], with a standard deviation of 1 μm. Most tracks of <17 μm lengths in other meteorites and in lunar samples lie between 10 and 13 μm, corresponding to tracks from iron nuclei. In ADR we looked for tracks of ≥3 μm but did not see any of <12 μm long in a sample of 257 fossil tracks (Fig. 2*a*, *b* and *c*). To estimate approximate values for the relative frequencies of short (and also long) tracks we sampled a large number of TINTs and TINCLEs. The results are given in Table 1. This type of analysis is not quantitative because we made an approximate estimate of the number of confined tracks in a given field of view and looked for tracks which had lengths different from the bulk. We conclude (see Table 1, Fig. 2) that $\leq10^{-3}$ of the fossil tracks in ADR are due to cosmic ray nuclei; the remaining tracks must be attributed to fission of uranium and transuranic elements.

The neutron induced track density in annealed ADR pyroxenes leads to a mean uranium concentration of 220 p.p.b. (based on 1,000 tracks counted). This value should be compared with the values of 170 ± 5 and 198 ± 5 determined by the neutron activation method[7,8], and 400 p.p.b. based on spark source mass spectrography[9] in the "whole" meteorite. This concentration of uranium would lead to only 6.2×10^{5} tracks/cm^{2},

Table 1 Limits on Areal Track Densities of Short and Long Tracks in Angra dos Reis

Track lengths of TINTs, TINCLEs	No. of confined tracks in a sample of about 5,000 TINTs and TINCLEs	Deduced approximate areal track density (cm^{-2})
<12 μm	5	10^{4}
>17 μm	18 *	4×10^{4}

* Length interval (μm)	17–18	18–19	19–20	20–21	21–22	22–23	23–24	24–25	25–26
No. of tracks	3	6	3	1	1	1	2	0	1

due to spontaneous fission of ^{238}U in 4.6 billion yr and thus the majority of the fossil tracks in ADR must be due to spontaneous fission of ^{244}Pu and ^{238}U. There is only 0.2 μm path difference estimated between the tracks of ^{244}Pu and ^{238}U. The estimated mean ratio of tracks due to ^{244}Pu and ^{238}U, $\rho\,(^{244}\text{Pu})/\rho\,(^{238}\text{U}) \simeq 19$. Our observations indicate that the concentrations of both ^{244}Pu and ^{238}U are quite variable from crystal to crystal as seen from Fig. 3. ^{244}Pu appears to be more uniformly distributed in comparison to ^{238}U since the fossil track densities vary over a factor of 1.8 as compared with neutron induced tracks which vary by a factor of 4.

The weighted mean lengths of fossil and neutron induced tracks are 14.36 and 14.32 μm, respectively (Fig. 3). A small difference, ~0.2 μm, would be expected in the two cases in view of the slightly different energy release. An important result of this comparison seems to be that over the life-time of the ADR meteorite as a solid body, the stored tracks have not been annealed to any measurable extent. In contrast, the recent results for terrestrial apatites of 0.4–1.2 billion yr age show large annealing effects of up to 10 μm (Bhandari *et al.*, unpublished).

The recorded ranges of fission fragments in ADR augite are identical to the observed neutron induced fission fragment track lengths in Kapoeta, Moore County, Nakhla and Steinbach. This is not at all surprising because the physical properties and compositional differences between various clino- and ortho-pyroxenes are such that the theoretically expected ranges of fission fragments are the same within ±0.5 μm (ref. 6).

Eighteen tracks (>17 μm) were found, some being as large as 26 μm. As discussed elsewhere[6], these tracks appear to be due to the spontaneous fission of super-heavy transuranic elements.

In Angra dos Reis the concentration of uranium in the pyroxenes is similar to that for the whole meteorite and thus it becomes meaningful to compare the fission contributions due to ^{244}Pu deduced from tracks with that based on analysis of the fissiogenic indicator isotope, ^{136}Xe. Analyses of Hohenberg[12] give a $^{244}\text{Pu}/^{238}\text{U}$ ratio that existed at the onset of xenon retention in ADR = 0.006. The expected $\rho\,(^{244}\text{Pu})/\rho\,(^{238}\text{U}) = 35$ which agrees well with the value of 19 estimated in the present work. The small difference may be attributed to a finite time lapse between the onset of xenon retention (~1,400° C) and that for tracks (500–600° C).

Finally, the observation of a cosmic ray track density of $\leq 10^4$ cm^{-2} is very intriguing considering that the cosmic ray exposure age of Angra dos Reis is 68 m.y.[11]. This value is based on the measurements of ^{3}He, ^{21}Ne and ^{38}Ar which lead to concordant ages, 66–70 m.y. ^{26}Al activity of 11.3 ± 9 d.p.m./kg, agrees with the expected value[14]. We deduce from the cosmic ray track density, the exposure age and the energy spectrum of iron group nuclei[3] that for most of its exposure period the ADR specimen was shielded by ≥ 30 cm in a body of ≥ 1 ton. The recovered mass, however, is only 1.5 kg and the simplest explanation would be a poor recovery or an unusually high ablation of $> \sim 99.9\%$ during atmospheric transit which is rare (unpublished results of Bhandari *et al.*). Alternatively one could invoke a recent breakup of ADR parent body in space; the post-breakup age of the recovered fragment would be 0.1, 0.3 and 1.0 m.y. for an effective shielding of 5, 10 and 15 cm respectively. A severe collision can, however,

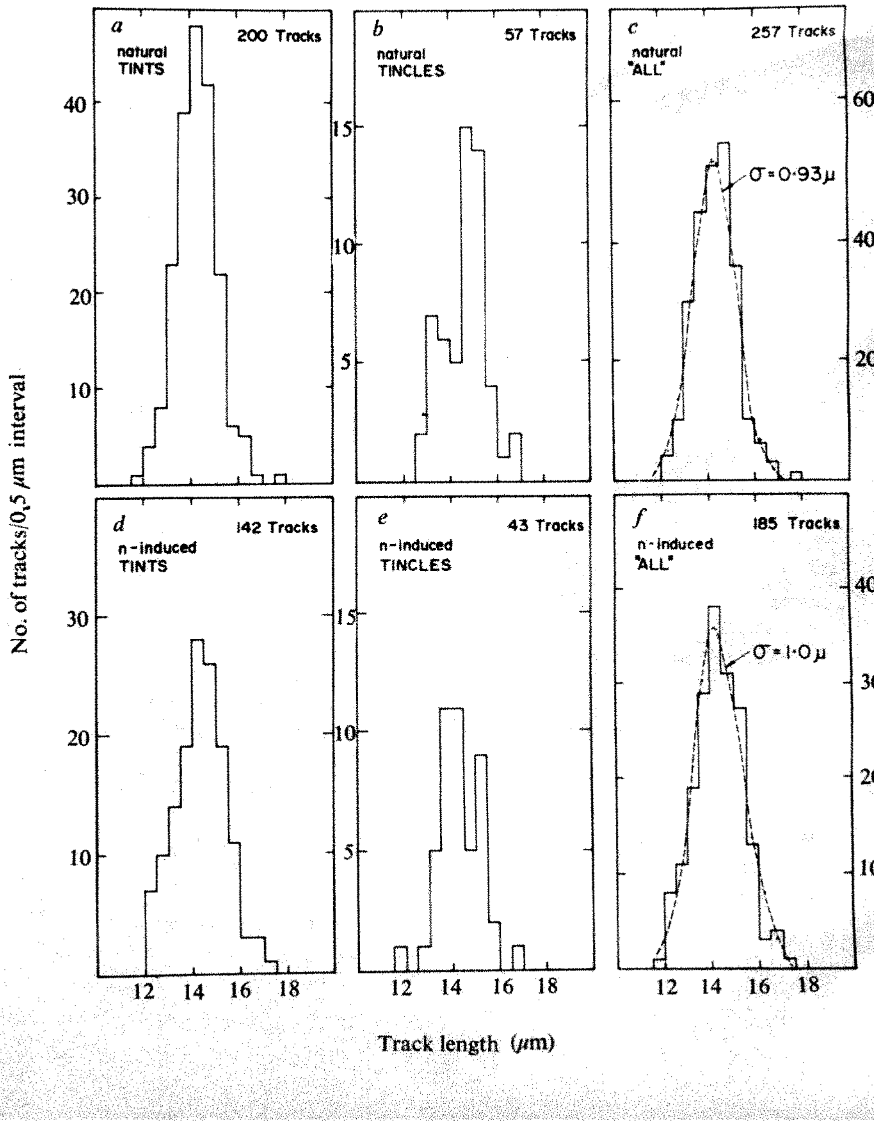

Fig. 2 Length distribution of confined tracks (TINTs and TINCLEs) in the meteorite, Angra dos Reis. *a*, *b* and *c*, Fossil tracks; *d*, *e* and *f*, neutron induced fission (^{235}U) fragment tracks.

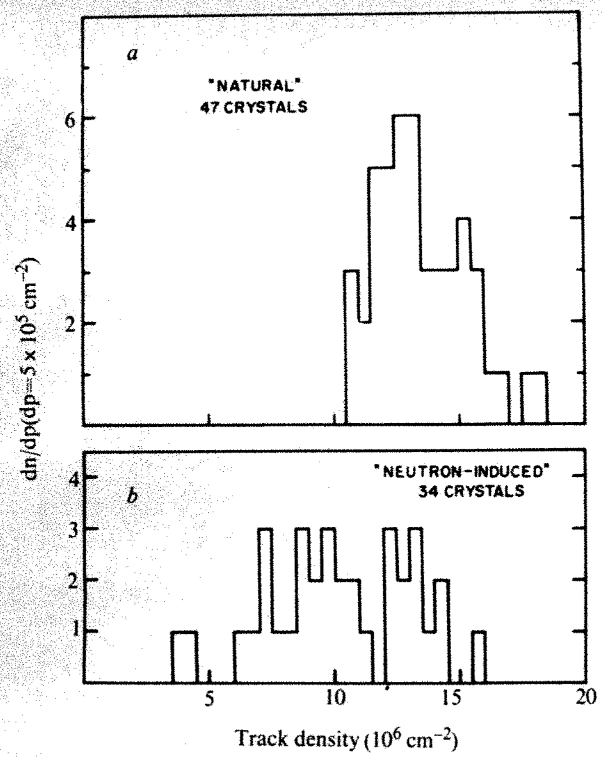

Fig. 3 Frequency distribution track densities in a random sample of Angra dos Reis crystals. *a*, Fossil tracks; *b*, n-induced tracks in an annealed sample.

be ruled out in view of the singular lengths of observed tracks and absence of annealing effects and gas losses.

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Experimental Decomposition of Algae in Seawater and Early Diagenesis

ALTHOUGH there have been many studies of organic decomposition processes in the marine environment and their effect on water chemistry[1–11], few geochemical investigations of these processes have been attempted in controlled conditions[12,13]. Our observations of organic decomposition in interstitial waters of carbonate sediments in Harrington Sound, Bermuda, prompted us to investigate these processes in the laboratory.

We report here changes in seawater chemistry produced by anaerobic bacterial decomposition of the marine algae *Caulerpa* sp. Laboratory results confirm the diagenetic trends observed in the composition of interstitial waters in modern anaerobic carbonate sediments, and suggest that the trends in water composition are primarily controlled by the interaction of decaying organic matter and seawater.

Samples of *Caulerpa* (1 g) were added to 150 ml. of seawater from filtered ('Millipore', 0.45 m) surface seawater, freshly collected from Ferry Reach, Bermuda, or anoxic seawater (unfiltered) collected from below the summer thermocline in Devil's Hole, Harrington Sound, Bermuda. Experiments were run in two series of six volumetric flasks each—one series for each water type. The containers were filled with solution before sealing (to avoid trapping any air other than that dissolved in the water), wrapped in aluminium foil and stored in the dark at room temperature.

Flasks were opened (one from each series) at intervals over 1 yr and analysed for *p*H, titration alkalinity, dissolved sulphides ($H_2S_{(aq)} + HS^-_{(aq)}$), and ammonia ($NH^+_{4(aq)} + NH_{3(aq)}$). Sulphides were determined by titration of excess iodine with sodium thiosulphate; ammonia was determined by the method of Richards and Kletsch[14], which also indicates labile amino-nitrogen.

Table 1 Compositional Changes of Seawater reacting with *Caulerpa*

Time (days)	Sample	*p*H	Alkalinity (mequiv. l.$^{-1}$)	$_mH_2S_{(aq)} + HS^-_{(aq)}$ $\times 10^3$	$_mNH^+_{4(aq)}$ $\times 10^4$
1	DH	7.50	2.69	0	ND
	FR	7.70	2.42	0	ND
30	DH	7.04	4.02	tr	0.7
	FR	6.99	4.90	tr	0.9
90	DH	6.74	7.42	2.0	3.3
	FR	6.74	8.55	2.6	2.9
150	DH	6.84	8.15	3.1	3.3
	FR	6.79	5.30	1.8	1.8
210	DH	6.99	5.50	1.4	1.7
400	DH	—	7.28	3.4	3.8

ND, Not detectable; tr, trace amounts; DH, sample seawater obtained from anoxic lower layer in Harrington Sound, Bermuda; FR, sample seawater obtained from oxygenated Ferry Reach lagoon, Bermuda.

Experimental data are presented in Table 1. The reactions in individual flasks proceeded at similar, but not identical, rates; no significant differences are evident between Ferry Reach and Devil's Hole water. The algae in these experiments decomposed rapidly by comparison with the rates of bacterial decomposition of organic matter in natural marine environments. After 30 days, the alkalinity had increased about 100%, almost 0.1 mmol of ammonia was present and the seawater

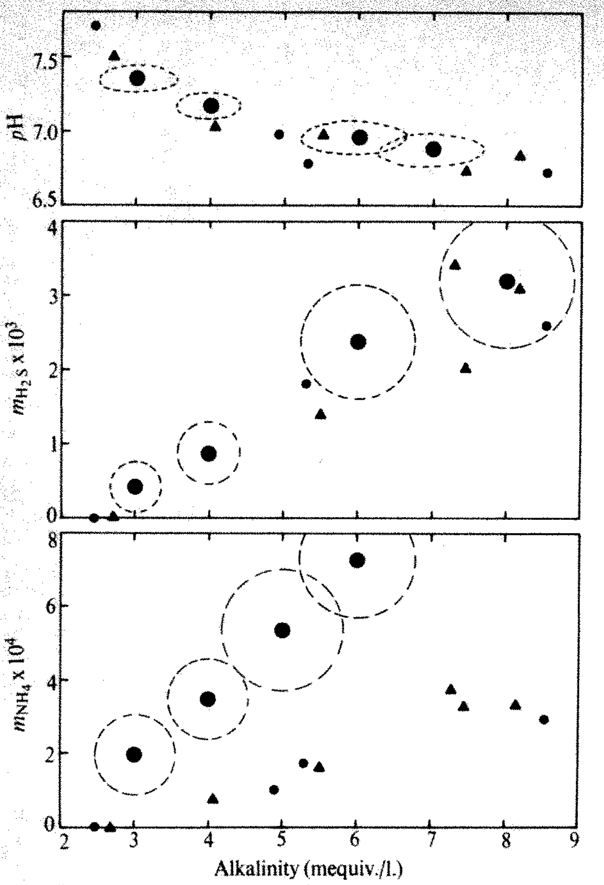

Fig. 1 Compositional variation of experimental solutions and interstitial waters of Devil's Hole carbonate sediments. Concentrations are expressed as molalities; m_{H_2S} represents the molality of total sulphide species ($H_2S + HS^-$). ▲, Experiments, Ferry Reach water; ●, experiments, Devil's Hole water; (●), Devil's Hole pore waters. Data points are mean values at depths of about 20, 40, 60, and 80 cm (left to right in the figure) from cores collected during summers of 1968 and 1970. - - -, Variability between cores.

contained traces of dissolved sulphide. After 1 yr, ~1% by weight of the algae was decomposed.

A generalized reaction for the decomposition process may be written

$$\text{Organic matter} + SO_4^{2-} \rightarrow CO_2, HCO_3^- + H_2S, HS^- + NH_4^+ \qquad (1)$$

The stoichiometric coefficients in equation (1) are a function of the ratio of C to N in the organic matter, the net oxidation state of the carbon in the organic matter and the pH at any given stage of the reaction. Equation (1) also shows that titration alkalinity provides a good estimate of the extent of the decomposition reaction, independent of reaction rate, as long as there is no significant solution or precipitation of carbonate or sulphide minerals in experimental or natural systems.

Fig. 1 compares our experimental results with data obtained from the interstitial waters of fine-grained, anaerobic carbonate muds in Devil's Hole, Harrington Sound, Bermuda[10,11]. There is no significant change in dissolved Ca^{2+} in the interstitial waters or in the experimental solutions, and there are no sulphide minerals in the Devil's Hole muds. Therefore titration alkalinity is used as a measure of the extent of decomposition. Fig. 1 shows that the changes in interstitial water chemistry run parallel to the experimental changes in solution chemistry. The differences in ammonia concentration probably reflect a difference in the ratios of C to N in the metabolized organic material or in the distribution of metabolized organic nitrogen between N_2 and NH_4^+ in the aqueous phase.

We have shown that, to a surprising extent, the effects of organic decomposition processes on the chemistry of marine waters in reducing environments may be theoretically modelled on the assumption of homogeneous equilibrium among the predominant dissolved species[9]. A necessary criterion for equilibrium is the equality of oxidation potentials for the various redox couples in the aqueous phase. Table 2 lists oxidation potentials for the redox couples $N_{2(aq)} : NH^+_{4(aq)}$ and $SO^{-2}_{(aq)} : HS^-_{(aq)}$, calculated from observed concentrations of aqueous species in the Devil's Hole interstitial waters and in our experimental solutions. The similarity of calculated oxidation potentials (pe_N and pe_S), independent of pH and solution composition, suggests that the dissolved species in both the pore waters and experimental solutions are approaching a state of homogeneous solution equilibrium.

Table 2 Oxidation Potentials computed for the Redox Couples $N_{2(aq)} : NH^+_{4(aq)}$ (pe_N) and $SO^{2-}_{4(aq)} : HS^-_{(aq)}$ (pe_S) *

Experiment					Devil's Hole carbonate muds †			
Time (days)	Sample	pH	pe_N	pe_S	Depth (cm)	pH	pe_N	pe_S
90	DH	6.74	−3.14	−3.27	10–26	7.28	−3.84	−3.76
	FR	6.74	−3.12	−3.30	26–38	7.20	−3.83	−3.71
150	DH	6.84	−3.27	−3.43	38–51	7.05	−3.68	−3.54
	FR	6.79	−3.11	−3.34	51–63	7.01	−3.63	−3.50
210	DH	6.99	−3.37	−3.55	63–76	7.00	−3.65	−3.49
					76–90	7.00	−3.66	−3.49

* For method of calculation, see ref. 9. Molality of dissolved N_2 assumed to equal saturation with air at 20° C.

† Data from ref. 9, page 761. Core No. 12, collected in summer 1968.

The variation of interstitial water chemistry with depth in the Devil's Hole carbonate muds has been closely reproduced as a function of time by our experiments, in which a marine algae decomposed in a closed chemical system. Observed concentration gradients of ammonia, sulphides and alkalinity in the Devil's Hole pore waters indicate, however, an upward transfer of dissolved species by diffusion. The similarity in composition between the experimental and pore solutions suggests that diffusion processes are removing dissolved species from the sediment in approximately the same ratios as they are produced by the decomposition reactions.

The decomposition rates in these experiments are comparable with reaction rates observed by Mackenzie *et al.*[15,16] for aluminosilicate minerals in seawater. These rates are geologically rapid and seem to be much higher than natural rates of organic decomposition in marine environments.

Our experiments, theoretical calculations[9] and field observations in Devil's Hole[10,11] indicate that, in a carbonate sediment, decomposition of organic matter by sulphate reducing bacteria will produce no significant solution or precipitation of carbonate minerals in spite of large changes in pH and solution composition. This does not eliminate the possibility of early diagenetic changes resulting from recrystallization of aragonite or magnesian calcites.

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Transported Aboriginal Artefact Material, Perth Basin, Western Australia

THE Perth Basin in south-western Western Australia contains numerous sites of surface and near-surface accumulations of rock flakes, and some of the material has almost certainly been carried for many hundreds of miles. The basin is filled with Proterozoic and Phanerozoic sediments, but outcrop is poor and large areas are covered by sand. In the east, the Perth Basin is bounded by the Precambrian Yilgarn Block, and in the south-west by the Precambrian Leeuwin Block. To the north lie the Precambrian Northampton Block and the sedimentary rocks of the Carnarvon Basin (see Fig. 1).

The rock flakes in the Perth Basin consist of bryozoan chert, non-fossiliferous chert, quartzite, dolerite, granite, K-feldspar, and other material, and usually range from less than 1 cm to 5 cm in diameter. The most prolific sites are blown-out areas near the tops of fixed dunes overlooking interdunal swamps and lakes. The rare presence of dolerite grinding stones and chopping tools in these accumulations confirms their Aboriginal origin, and the frequent presence of broken glass and china at some sites seems to show that they were used after European occupation.

All fragments of dolerite, granite, quartzite and non-fossiliferous chert have come from Precambrian terrains, and the nearest source to some artefact sites is about 40 miles away. The bryozoan chert, on the other hand, has apparently come much farther.

Bryozoan chert is present at almost all blown-out sites found in the Perth Basin, and at some sites comprises more than half of the material. It is a silicified, aphanitic bryozoan limestone, and its property of breaking with conchoidal fracture into hard, sharp flakes would have been useful to Aborigines, and doubtless accounts for its wide distribution. The following Bryozoa have been recognized: Ascophoran new gen. and sp., *Aspidostoma clarkei* (Woods), *Arachnopusia ferrea* (Waters), *Crateropora* sp., *Cribrilaria* sp., *Foveolaria savartii* (MacGillivray), *Ogiva* sp., *Porina gracilis* (Lamarck), *Schizophoria vigilans* Waters, *Sertella mucronata* (Waters), *Acerinucleus* sp., *Cellaria* spp., *Celleporaria tridenticulata* (Busk), *Membranipora* cf. *cyclostoma* MacGillivray and *Tubitrabecularia elevata* (Woods). The Eocene age indicated by the Bryozoa is confirmed by the presence in two chips of the Middle and Upper Eocene foraminifer *Maslinella chapmani* Glaessner and Wade. There are also some sponge remains.

The bryozoan chert cannot be matched with formations in either the Perth Basin or the Carnarvon Basin and, because no Eocene bryozoan limestones are known offshore, a western source is unlikely. Silicified rocks from four Eocene rock units in southern Western Australia resemble the artefacts. These units are Plantagenet Group[1] and Norseman Limestone[2] which overlie the southern Yilgarn Block in patches, Toolinna Limestone[3,4] farther east, and Wilson Bluff Limestone[3,4] exposed at Wilson Bluff near Eucla, and in caves in that area. Flint artefacts from Wilson Bluff have been recorded near Eucla[5,6], and their use apparently continued into the ethnographic present[7]. Geologically similar material had been quarried in Koonalda Cave, 60 miles east of Eucla, which has been shown to have been in use from between 20,000 and 13,000 yr ago[8].

It is not possible at present to specify the source of the artefacts or their mode of transportation. If the chert came from the

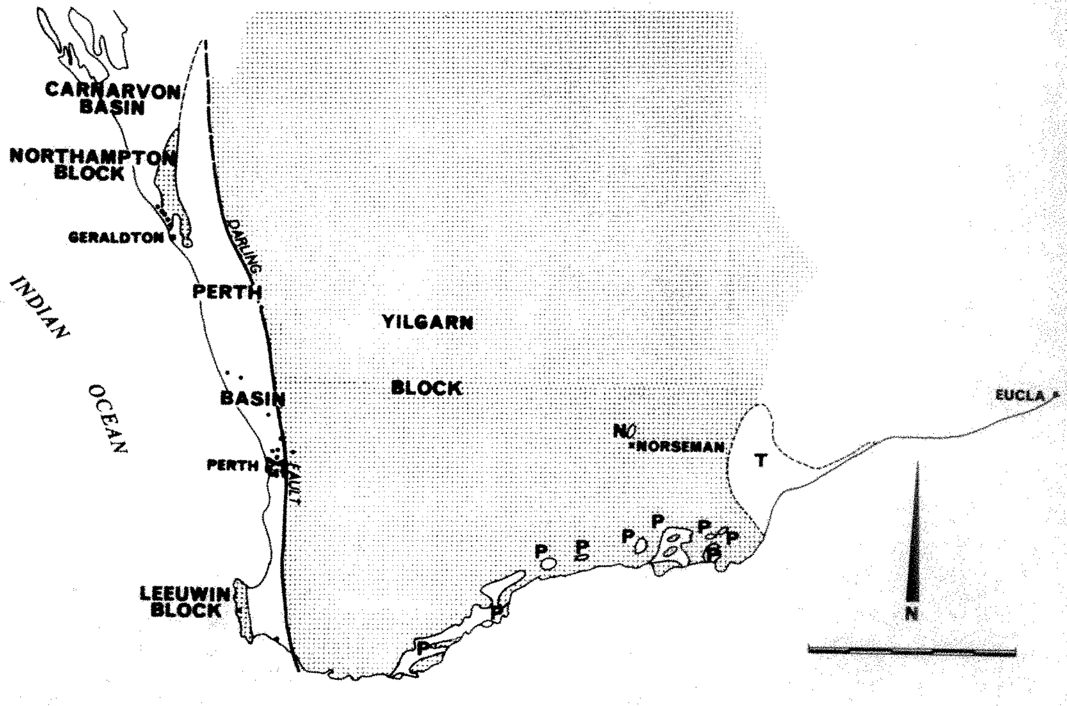

Fig. 1 Map of south-western Western Australia. Dots show artefact sites containing bryozoan chert. *P*, Plantagenet Group; *N*, Norseman Limestone; *T*, Toolinna Limestone. Bar scale 200 miles, divided into 40 mile intervals.

most westerly of these possible source rocks (Plantagenet Group) it was carried at least 500 miles to sites in the north of the Perth Basin. Studies of the distribution of this distinctive rock may throw light on former Aboriginal trading patterns and tribal interrelationships.

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BIOLOGICAL SCIENCES

Resolution of a Paradox with After Images

Two weeks ago I described the results of flash bleaching the retina with a bright uniform field seen through a set of neutral filters as shown in Fig. 1*b*. Ten minutes later cones had quite recovered and only rods contributed to the after image. This was observed by briefly opening the eyes from time to time and looking at a faintly illuminated white wall. After 20 min the negative after image looked as shown in Fig. 1*e*, and at later times it gradually faded in its black contrast to the white wall. But at earlier times the image did not get continually more intense; it exhibited a ceiling of intensity and no segment could exceed the intensity of sector C at 20 min.

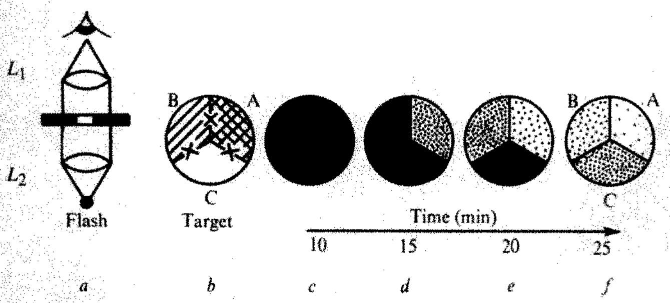

Fig. 1 *a*, Electronic flash collimated by lens L_2 and presented to eye in Maxwellian view by L_1. Interposed mid-way is the tripartite filter shown in *b*. Sectors A, B, C are neutral densities 1.2, 0.6, 0.0 respectively. The centre is fixated and areas A, B, C of retinal image differently bleached. *c–f* represent the appearance of the negative after image seen by momentarily opening the bleached eye and viewing a faintly illuminated white wall. At 10 min (*c*) the image is uniformly black; at the subsequent times shown, it breaks up into sectors and gradually fades in blackness.

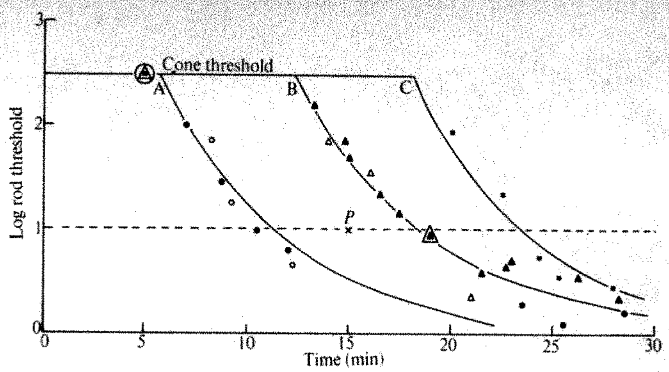

Fig. 2 Black symbols plot the rod dark adaptation curves A, B, C when the test flash fell near the middle of bleached areas A, B, C respectively (Fig. 1*b*). Threshold is measured as log luminance of wall seen through a hole in a screen. White symbols (curve A) plot log luminance of wall just sufficient to make sector A, Fig. 1*b*, distinct from B in the negative after image. In curve B the white symbols plot log luminance to make sector B distinct from C.

This abrupt ceiling of intensity seems surprising, for we expect the dark adaptation curve to follow the fading in intensity of the after image, and for each of the three sectors A, B and C the dark adaptation curve shows no sudden flattening (Fig. 2) (except, of course, for the cone-rod break which is not here involved). To display the relation between after images and dark adaptation we employed the very simple arrangement of Fig. 3.

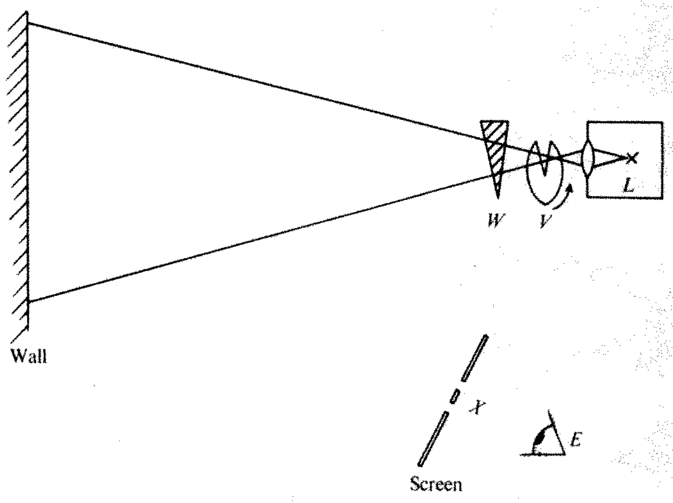

Fig. 3 Arrangement for comparing thresholds and after images during dark adaptation. Light is projected from *L* onto a white wall, interrupted (0.5 s on, 3.5 s off) by rotating vane, *V*, and attenuated by the wedge, *W*. The eye at *E* observes the light flashing from the wall either (i) through three holes in the screen *S* so placed that, when *X* is fixated, light falls on the three bleached regions, Fig. 1*b*; or (ii) by removing the screen and viewing the negative after image against the intermittent light from the wall.

The white wall is illuminated by a lamp, *L*, with light attenuated by a grey wedge, *W*, and interrupted by a rotating vane, *V*, on for 0.5 s and off for 3.5 s. The observer, with eye in fixed position *E*, could see the negative after images on the wall each time the vane lit it up, except when the black screen, *S*, was interposed. The screen was pierced with three small holes so placed that when the eye fixated on the tiny red light, *X*, the flashing holes were seen about in the middle of the three sectors A, B, C of the after image.

It is plain that this situation is in effect the ordinary arrangement for plotting dark adaptation curves, and the three curves of Fig. 2 were so obtained (black symbols). At various times in the dark while *X* was being fixated, hole A or B or C was observed flashing, and the wedge adjusted so that the flashing just disappeared. By transferring attention to A, B and C at appropriate times, the three curves of Fig. 2 were obtained at a single run.

To resolve the paradox, suppose that at 15 min of dark adaptation we turn up the illumination of the wall to the level, *P*, Fig. 2. This brightness is below threshold for B and C, but above threshold for A; consequently when we remove the screen and look at the wall we expect B and C to be unstimulated and thus fully black (as it was when observed through the hole in the screen) but that A should be lighter, though less bright than the surrounding wall whose image falls on completely unbleached retina. We expect then to see an appearance like Fig. 1*d* and that is what we do see. If the light on the wall is of fixed brightness (as in the previous experiments) the point *P*, Fig. 2, will move with time along the horizontal dotted line and cross in succession the three curves. At the moment of crossing A, suddenly sector A of the negative image becomes brighter than the fully dark B and C; at the moment of crossing curve B, sector B becomes suddenly brighter than C (though still remaining dimmer than A). This accounts for the previous observation that each sector rises from full blackness at the moment when its dark adaptation threshold had reached a fixed critical value. We now see that that fixed value was simply the brightness of the wall against which the negative image was seen.

In the present experiment we need not wait for dark adaptation to reach the fixed critical wall value, for at any moment we may adjust the wall luminance to be critical for that state of adaptation. The white symbols in Fig. 2 show the luminance at which the intensity of two segments is just noticeably different. Except near complete recovery the dark adaptation threshold is the same as that for detecting a luminance difference between segments. Near complete recovery it is easier to detect the slight difference between full darkness and something a shade lighter when viewing the whole segment than when sampling it through a small hole.

In conclusion, the ceiling of blackness in negative after images results not from any limitation inherent in after image brightness, but simply from the fact that negative brightness cannot become more intense than full blackness.

Consequently these results with negative images in no way contradict the conclusions of Barlow and Sparrock that during dark adaptation the threshold is raised because the positive after image acts in the same way as a luminous background of equal brightness.

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Increased Incidence of Rous Sarcomas in Response to Excess Vitamin A

VITAMIN A influences cell differentiation and can produce metaplasia of squamous and mucous secreting epithelia[1-3]. It is also mitogenic[4,5] and influences epithelial tumorigenesis[6,7]. Previous studies[6,8] have demonstrated the co-carcinogenic effect of topical vitamin A palmitate during chemical carcinogenesis in the hamster cheek pouch. We wish to report the effect of topical vitamin A palmitate on Rous sarcomas in chickens.

A tissue culture stock of the Schmidt-Ruppin strain of Rous sarcoma virus (SR-RSV) was prepared by infection of 9 day old chick embryo fibroblasts. Culture medium 199 with 5% inactivated calf serum and 10% tryptose phosphate was used (Gibco). The medium was collected 7–10 days later and stored at 70° C until used. Twenty 4-month-old White Leghorn chickens were injected in both wing webs with different amounts of RSV which originally titred 10^5 focus forming units (f.f.u.) $\mathrm{ml.}^{-1}$. Amounts injected ranged from 5,000–20,000 f.f.u. (Table 1). One day after the injection of the virus, the right wing webs (RSVA webs) were treated topically with a 20% solution of vitamin A palamitate in paraffin oil USP daily for three weeks (vitamin A palmitate, Merck, Darmstadt, 1.7 million, 1 U g^{-1}). The left wing webs were left untreated (RSV webs).

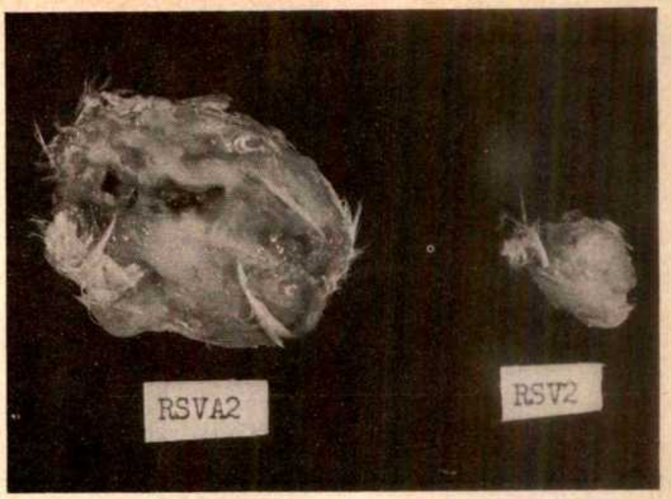

Fig. 1 Comparison in size of tumours obtained after injection of virus only (RSV) and after injection of the virus followed by topical application of vitamin A palmitate (RSVA).

Six birds (A group), received topical application of vitamin A palmitate only for 3 weeks in an identical manner. The right wings of another six birds (P group) were treated with paraffin oil daily for 3 weeks after the injection of RSV. After 3 weeks, the animals were killed and the tumours excised, measured and weighed, and examined histologically.

Table 1 Incidence, Size and Weight of Tumours after Injection of RSV with and without Subsequent Topical Application of 20% Vitamin A Palmitate

	No. of	No.with	% with	Tumours	
Group	animals	tumour	tumour	Diameter	Weight
RSV only 5,000–20,000 f.f.u.	20	3	15%	1/2–2 cm	4–6 g
RSV 5,000–20,000 f.f.u. + vitamin A	20	10	50%	1–6 cm	4–50 g

The results of the experiments are summarized in Table 1. The results in the P group were essentially the same as those obtained in RSV webs and are thus not described separately. Topical application of vitamin A eventually resulted in induration of the entire web and histologically these areas showed marked epidermal hyperplasia with focal atypia.

In the RSVA webs tumours became obvious macroscopically before RSV web tumours. Of the 20 RSV wing webs, only three showed tumours weighing up to 6 g with a maximal diameter of 1–2 cm. Ten tumours developed in RSVA wing webs weighing up to 50 g and measuring up to 6 cm in diameter (Fig. 1). RSVA tumours were partially necrotic and often infiltrated the entire wing.

The histology of RSV tumours showed fibrosarcoma of low grade malignancy containing only small amounts of mucinous material.

The histology of the RSVA tumours revealed a much more malignant fibrosarcoma containing myxomatous elements. The individual tumour cells were more rounded with nuclear hyperchromasia and the stroma contained abundant mucopolysaccharides. There was also direct invasion of muscle.

Vitamin A enhanced the malignant growth and increased the incidence of sarcomas producing more anaplastic tumours. This enhancing effect of vitamin A has been demonstrated during hamster cheek pouch carcinogenesis and in rabbit keratoacanthomas[6,7,8-10]. Little is known of its effect in viral tumorigenesis, other than a reported increased incidence of avian leukosis in response to excess dietary vitamin A[11].

The effects of vitamin A on cell division, mitotic activity[4,12] and membrane labilization are well recognized[13,14], and its co-carcinogenic effect was attributed to these qualities of the vitamin[6,8,9]. It was suggested that as a result of increased cell membrane permeability chemical carcinogenes entered the cell more easily and acted more effectively. This membrane effect probably underlies the appearance of metastasis in spontaneous mammary tumours in response to excess vitamin A[15]. Thus in our experiments, the virus may have been able to penetrate the cell more effectively with consequent earlier and more expensive development of tumours.

Furthermore, vitamin A excess increases malignant transformation and mitotic rate of cultured fibroblasts[16] and is known to alter the shape and structure of certain viruses[17]. This is due to absorption of the vitamin to the viral membrane with consequent alteration of the bimolecular lipid leaflet. Alteration of the structure and function of the virus and the target cell (the fibroblast) by the vitamin may also be contributory factors in the enhancement of malignancy in this study.

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Amino-acid Contamination of Aqueous Hydrochloric Acid

SIDLE[1,2] has drawn attention to the contamination of aqueous HCl, both undistilled and distilled, by amino-acids. This is an important problem, for example, when HCl is used to hydrolyse material such as lunar and meteorite samples which contain very small concentrations of amino-acids and peptides. We have obtained data on the amino-acid contamination of distilled constant boiling HCl which we believe to be due to the volatility of the amino-acids in aqueous hydrochloric acid.

We found considerable amino-acid contamination in commercially available analytical grade hydrochloric acid (37% HCl). One bottle (Allied Chemical) contained 8,300 nmol of amino-acids per l.; another (Baker) contained 6,700 nmol per l. The contaminants were mostly protein amino-acids and several unknowns. The samples were diluted 1:1 with glass distilled water and distilled to form constant boiling HCl[3-5]. The product contained 47 to 83 nmol of amino-acids per l. Contamination was caused by the volatility of the amino-acids.

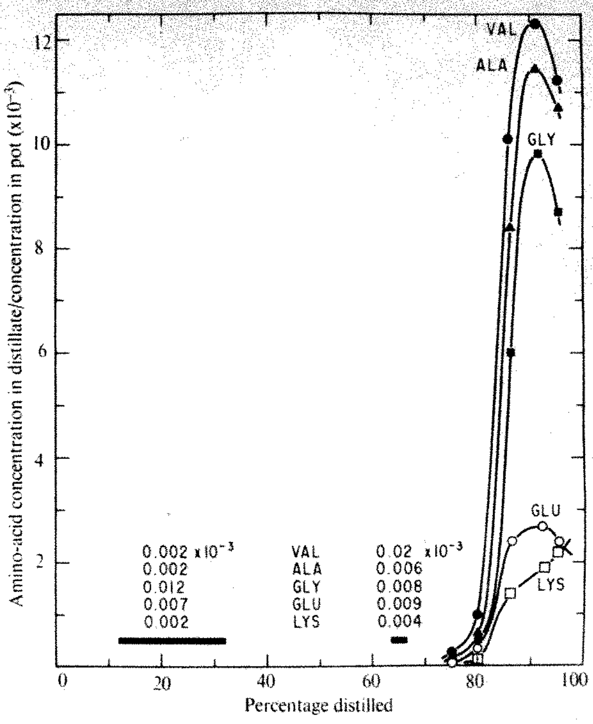

Fig. 1 The ratio of the amino-acid concentration in the distillate to the amino-acid concentration in the pot as a function of the per cent distilled. The numbers on the left are the average between 12 to 32% distilled; the ones on the right are the average between 63 to 67% distilled.

To obtain data on the volatility of the amino-acids during the HCl distillation, we distilled constant boiling HCl with known amounts of various amino-acids and determined the amounts of the amino-acids in the distillate. Constant boiling HCl (4 l.) containing 4 mmol each of valine, alanine, glycine, glutamic acid and lysine was distilled from a Claisen flask with two Kjeldahl bulbs. The flask was heated by an electric heating mantle, and the distillate was collected at a rate of 350 ml./h. Various fractions were evaporated to dryness in a vacuum desiccator and the residue was run on an amino-acid analyser.

The ratio of the amino-acid concentration in the distillate to that in the pot is shown in Fig. 1. The amino-acid contamination becomes a serious problem in the last quarter of the distillation. This is an important point since the instructions for preparing constant boiling hydrochloric acid call for the distillation of an approximately 6 M HCl solution, rejecting the first three quarters of the distillate and collecting the remainder except for a residue of about 5% (ref. 5). This may account for the amino-acids Sidle found in his distilled HCl (refs. 1, 2).

The fact that the ratio of amino-acids in the distillate to the amino-acids in the pot is not constant implies that the amino-acids are not being distilled in a simple manner. The problem is not caused by the transfer of amino-acids in the spray because the data in Fig. 1 show that the amino-acids have different volatilities. Our explanation is that some of the amino-acids dry out on the sides of the flask as the liquid level in the still falls. The solid amino-acid hydrochlorides are carried over by the rapid flow of vapours through the still.

It is clear from these data that the first half of the HCl distillate should be collected rather than the last quarter. Even then there is some amino-acid contamination.

To obtain 6 M HCl free of amino-acids, we use the following method. Gaseous HCl (Matheson, electronic grade) is condensed with liquid nitrogen, weighed, and transferred through a vacuum line to the required volume of glass distilled water.

By using this method we obtain 6 M HCl which contains less than 0.2 nmol of amino-acids per l.

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Amplifying and Suppressive Effect of Thymus Cells

THE humoral immune response against a variety of antigens in mice requires the interaction of an antibody forming precursor cell derived from bone marrow (AFPC) and a thymus-derived helper cell[1-3]. In the chicken, plasma cell formation and immunoglobulin synthesis are ontogenetically controlled by the bursa of Fabricius[4], suggesting that in this species the bursa provides the AFPC, but it is not clear what role the thymus plays in the humoral antibody production. Neonatal thymectomy of chickens does affect antibody formation, at least towards some antigens[5,6]; and by analogy with mice[7,8] thymus dependency varies strongly with the antigen dose and also with respect to the class of antibody affected (W. D., and Malchow, D., unpublished work). Attempts to demonstrate a synergistic effect between thymus and bursa cells in the chicken, however, have not been successful[7,10]. I wish to describe experiments indicating that thymus cells can cooperate with a bursa-dependent component in the production of agglutinating antibodies and also that in a different experimental situation thymus cells show a suppressive effect on antibody formation.

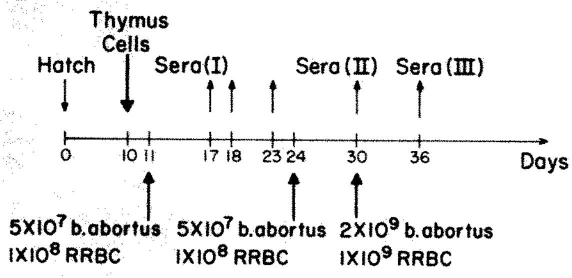

Fig. 1 Experimental schedule.

The experimental schedule is outlined in Fig. 1. Thymus cells were isolated from 8 week old Leghorn chickens which were F_1 hybrids between two inbred strains identical with respect to the major blood group histocompatibility locus (B^2/B^2). (Eggs were provided by Dr G. R. J. Law.) Between 10^7 and 5×10^7 thymus cells from normal (TN) or neonatally bursectomized (Tbx) donors were injected intracardially into 10 day old normal or neonatally bursectomized chickens of the same line. All animals were immunized 1 day later with 5×10^7 *Brucella abortus* organisms (US Department of Agriculture, Ames, Iowa 50010) and 1×10^8 rabbit erythrocytes (RRBC) intraperitoneally. Serum samples (series I) were taken 6, 8 and 12 days after immunization and titrated on disposable microtitre plates (Cooke Engineering Co., Alexandria, Virginia) for agglutinating antibodies against *Br. abortus* and RRBC[10,11].

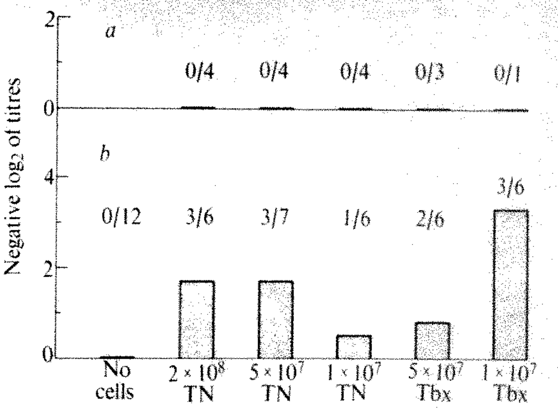

Fig. 2 Anti-*Brucella abortus* titre after first immunization (day 11) (sera of group I in Fig. 1). The bars represent the means of the negative $\log_2$ of the titres. (Sera which showed no agglutination in the first well were always included in the mean as 0.) The numbers give the proportion of responding animals per total animals in the group. TN, birds received thymus cells from normal donors. Tbx, birds received thymus cells from bursectomized donors; *a*, bursectomized recipients; *b*, normal recipients.

The 10 day old chickens, whether untreated or neonatally bursectomized, gave no detectable response against *Br. abortus* (Fig. 2), and only a few normal animals responded against RRBC (Fig. 3). Experimental groups which had received thymus cells, however, showed a significant proportion of responding animals. In one group (1×10^7 Tbx), the responding animals gave titres up to $1:2^9$. The non-responding animals in these groups were not identical with respect to the two antigens. For example, in a group of six animals, two responded to both *Br. abortus* and RRBC, two responded to one or the other antigen, and two gave no detectable response to either antigen. When the same number of thymus cells was injected into 10 day old neonatally bursectomized birds, no detectable response was found in any of the recipients against either antigen. The thymus cells apparently cannot provide a response by themselves, but need a bursa-dependent component in the recipient. Administration of thymus cells from bursectomized donors (Tbx) resulted in titres to either antigen as good as or even better than thymus cells from normal animals (TN). Tbx cells also resulted in a better immunological memory as seen by the response to a second and third immunization 14 and 20 days after cell transfer (schedule of Fig. 1). While the Tbx recipients still showed higher responses than the controls, the TN recipients gave comparably low titres, in some cases even lower than the normal controls which had received medium instead of cells (Tables 1 and 2).

A strong suppressive effect on the formation of agglutinating antibody was observed when 5×10^7 thymus cells from 6 week

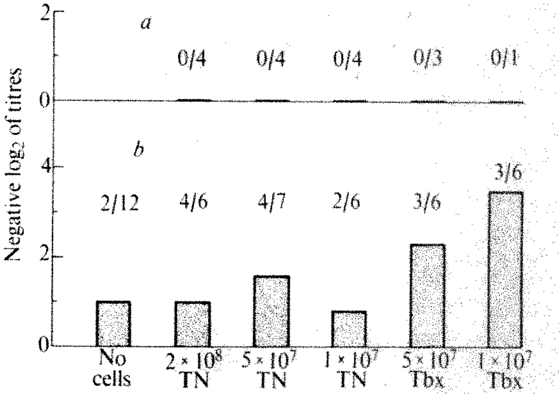

Fig. 3 Anti-RRBC titre after first immunization (day 11) (sera of group I in Fig. 1). See legend to Fig. 2. *a*, Bursectomized recipients; *b*, normal recipients.

Table 1 Anti-*Brucella abortus* Titre after Second (Day 24) and Third (Day 30) Immunization (Sera of Groups II and III in Fig. 1)

	Second			Third		
Birds received at day 10	Total titre	ME-resistant titre	Total titre		ME-resistant titre	
Only medium	7.8	0.0*	10.8		5.6	
5×10⁷ TN	6.6	0.4	10.0		1.9	
1×10⁷ TN	7.0	3.0	11.2	$P<0.15$	3.7	$P<0.025$
5×10⁷ Tbx	8.8	1.5	12.8		6.2	
1×10⁷ Tbx	9.7	1.0	15.8		6.5	

Data are expressed as means of the negative $\log_2$ of the titre. * Negative sera are included in the mean as 0.

Table 2 Anti-Rabbit RBC Titre after Second (Day 24) and Third (Day 30) Immunization (Sera of Groups II and III in Fig. 1)

	Second			Third			
Birds received at day 10	Total titre	ME-resistant titre		Total titre		ME-resistant titre	
Only medium	8.4	5.8		7.8		7.0	
5×10⁷ TN	8.7	4.0		7.6		6.4	
1×10⁷ TN	10.2	6.8	$P<0.0005$	9.2	$P<0.20$	8.0	$P<0.06$
5×10⁷ Tbx	12.0	9.3		10.4		9.4	
1×10⁷ Tbx	10.5	6.5		10.8		8.5	

Data are expressed as means of the negative $\log_2$ of the titre.

old donors were given intravenously to immunologically mature 6 week old recipients, which were again immunized with 5×10^7 *Br. abortus* organisms and 1×10^8 RRBC, intraperitoneally, 1 day later. Sera were obtained 6, 8 and 12 days after immunization. Total titres, as well as ME-resistant titres (titrated in the presence of mercaptoethanol), against both *Br. abortus* and RRBC were substantially decreased in birds which received 5×10^7 TN, while recipients of 5×10^7 Tbx gave practically the same response as the normal controls (Figs. 4 and 5). The standard errors of the mean titres were relatively high in some of the experimental groups, but the suppressive effect was in general statistically significant (Table 3). The total titres were on the average sixteen times (2^4) stronger than the ME-resistant titre (IgG), so they can probably be regarded as IgM titres. The results (Tables 1 and 2) indicate that a suppressive effect is still observed 3 weeks after the original cell transfer and after repeated immunizations. The most significant reduction in the antibody response of TN compared with Tbx recipients was seen in the ME-resistant titres. *P* values were calculated by the Student *t* test.

Thymus cells thus seem both to amplify and to suppress the production of agglutinating antibody in the chicken. The former effect, however, was unaffected by neonatal bursectomy of the thymus cell donor, whereas the latter was "bursa-dependent".

The nature of the cooperative (amplifying) effect is unknown. In analogy to the thymus cell–bone marrow cell cooperation in mice[1-3], it might be explained as the cooperation of thymus cells with a bursa-dependent AFPC, for the bursa is known to control plasmacyte formation in chickens[4]. This interpretation implies that the 10 day old chicken still has a deficient thymus-dependent system but already has appreciable amounts of AFPC. In this sense, it serves as a substitute for neonatally thymectomized chickens. The high proportion of thymus cell recipients with no detectable response, however, may indicate that the bursa-dependent AFPC component is not completely mature at this time. The observation that some of the thymus cell recipients cannot respond to one antigen but do respond to the other, and vice versa, indicates that the thymus cells have been transferred successfully and are active.

The suppressive effect, in contrast to the amplifying activity, is more strongly expressed after transfer of thymus cells to the immunologically mature 6 week old chicken than to the 10 day old bird and is not obtained with thymus cells from neo-

Table 3 Statistical Analysis of the Suppressive Effects shown in Figs .4 and 5

	Controls	Birds received 5×10⁷ Tbx	 5×10⁷ TN	*P* value (Student *t* test)
Anti-*Brucella abortus*				
Total	6.4±1.1	8.0±2.2	1.2±0.7	<0.02
ME-resistant	2.7±1.0	3.8±1.8	0.0±0.0*	<0.08
Anti-RRBC				
Total	8.4±0.8	9.2±1.0	5.8±1.0	<0.05
ME-resistant	4.8±1.0	4.8±1.0	1.4±0.4	<0.015

Data are expressed as means of the negative log 2 of the titres (±s.e.). The 13 day sera of Tbx and TN recipients are compared by the Student *t* test. * Negative sera were always included in the means as 0.

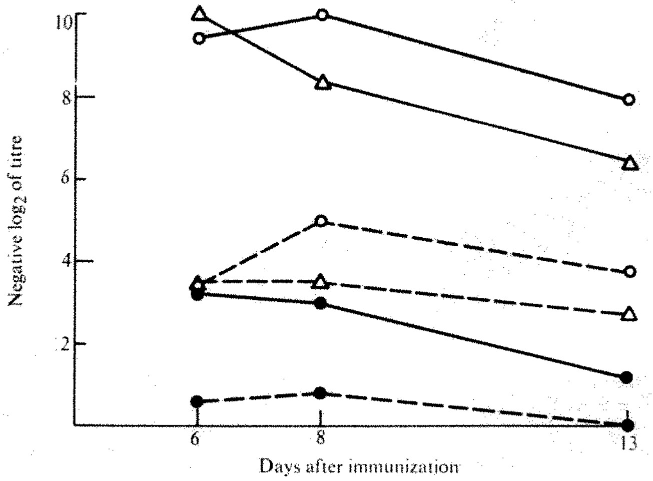

Fig. 4 Anti-*Brucella abortus* agglutinin titre of chicken after transfer of thymus cells at 6 weeks of age. The chickens were immunized with 5×10^7 *Brucella abortus* organisms and 1×10^8 RRBC 1 day after cell transfer and the sera collected 6, 8 and 13 days after immunization and assayed by microtitre agglutination[10,11]. ——, Total titre; - - - - -, ME-resistant titre; △, normal control; ○, recipients of Tbx; ●, recipients of TN.

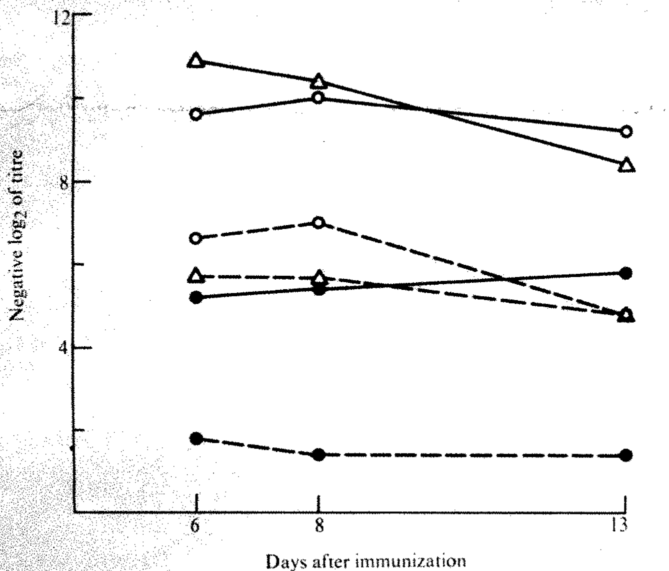

Fig. 5 Anti-RRBC agglutinin titre of chicken after transfer of thymus cells at 6 weeks of age. See legend to Fig. 4.

natally bursectomized donors. A suppressive effect has not been observed after transfer of syngeneic thymus cells to normal mice[12]. But the suppressive effect described here may resemble that found in mice treated with anti-lymphocyte serum[13]. More information, particularly on the antigen specificity of the suppression, is necessary to test the possible relevance of this effect to specific immunological unresponsiveness (tolerance) or related phenomena.

We have previously reported the existence of two different sub-populations of cells in the chicken thymus as defined by their electrophoretic mobility[14]. One of these two populations was missing in neonatally bursectomized birds. This "bursa-dependent" population may be the carrier of the suppressive effect. The other population which is not bursa-dependent apparently must have the ability to provide the thymus-dependent cell mediated immune functions as well as cooperate in the humoral response, at least in the formation of agglutinating antibody.

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Inhibition of Methanogenesis by DDT

Methanobacterium strain M.o.H. is a strict, anaerobic methane-forming bacterium which obtains its energy from the oxidation of hydrogen; the electrons generated are passed to CO_2 which is reduced to CH_4. Inhibition of CH_4 biosynthesis by alkyl halides was first documented by Bauchop[1] who reported that the addition of carbon tetrachloride, chloroform or methylene chloride to rumen fluid inhibited CH_4 production and increased H_2 production. Rufener and Wolin[2] reported similar findings in an artificial rumen system. Van Nevel[3] described the inhibitory effects of chloral hydrate on CH_4 formation in sheep rumen fluid incubated *in vitro* and *in vivo*. These observations were extended by Wood[4] who described the inhibitory effects of chloroform, dichloromethane, methylene chloride and propyl iodide on CH_4 formation in cell extracts of *Methanobacterium omelianskii*. Photolysis was observed to reverse inhibition. The site of action of these compounds has not been identified, but the reversal of inhibition by light was taken as evidence that the site is a B_{12} complex involved in the final transmethylation reactions which lead to CH_4 synthesis[4]. The similarity between chloroform and the active centre of 1,1,1,trichloro-2,2 *bis* *p*-chlorophenyl ethane (DDT) raised the possibility that this pesticide might also inhibit methane biosynthesis.

Methanobacterium strain M.o.H. was grown as described by Bryant[5]. Cell-free extracts were prepared by the procedure of Roberton[6]. Methyl cobalamin (CH_3–B_{12}) was prepared as described previously[7]. DDT and DDT-derivatives were supplied by Dr R. L. Metcalf. The pesticides were dissolved in dimethylformamide. Appropriate amounts of dimethylformamide were always added to control flasks. Assays were performed as described by Wolin[8]. Methane was measured in a Packard gas chromatograph equipped with silica gel column and a hydrogen flame detector. Whole cells were suspended in their growth liquor.

The effects of DDT on CH_4 formation in cell-free extracts are shown in Fig. 1*A*; 10^{-6} M DDT inhibits the reduction of CO_2 to CH_4 by 75%. In view of the large amount of cell extract used in these experiments (35 mg protein/ml.) and of the resulting high probability of non-specific adsorption, DDT is a potent inhibitor of CH_4 formation. Whole cells require twelve times as much DDT to inhibit CH_4 formation to the same extent (Fig. 1*B*). The decreased sensitivity of whole cells may result from an inability of DDT to efficiently permeate intact cell membranes. Similar concentrations of DDT were found to inhibit the reduction of formate to CH_4 by whole cells of *Methanobacterium ruminantium* strain P.S.

1,1,Dichloro-2,2, *bis* *p*-chlorophenylethane (DDD) inhibits CH_4 biosynthesis in cell extracts (Fig. 1*C*) but is much less effective than DDT. The effect of several DDT derivatives and cyclodienes on CH_4 synthesis is described in Table 1. DDD is active only in cell extracts, presumably it does not enter whole cells. 1,Chloro-2,2 *bis* *p*-chlorophenylethylene (DME) and 1,1,dichloro-2,2 *bis* *p*-chlorophenylethylene (DDE) have no effect on either cell extracts or whole cells. Methoxychlor, a DDT derivative in which the ring chlorines are replaced with methoxy groups, is a strong inhibitor, only slightly less active than DDT. The three cyclodienes examined had no effect on CH_4 formation.

Table 1 Effect of Various Chlorinated Insecticides on CH_4 Biosynthesis in Cell Extracts and Whole Cells of *Methanobacterium* Strain M.o.H.

Addition	Cell extract Molarity of insecticide	Cell extract μmol CH_4	Cell extract Inhibition (%)	Whole cells Molarity of insecticide	Whole cells μmol CH_4	Whole cells Inhibition (%)
None	—	26.4	0	—	4.8	0
DDT	1×10^{-6}	6.6	75	3×10^{-5}	0.63	87.0
DDD	5×10^{-5}	15.8	40	1×10^{-4}	4.9	0
DDE	1×10^{-4}	25.1	5	1×10^{-4}	4.7	0
DME	1×10^{-4}	25.4	4	1×10^{-4}	5.0	0
Methoxychlor	3.3×10^{-6}	10.8	59	3×10^{-5}	2.9	40
Cyclodiene	1×10^{-4}	26.3	0	1×10^{-4}	4.7	0

Cell extract reaction flasks contained: TES buffer, *p*H 7.0, 200 μmol; adenosine triphosphate, 10 μmol; crude cell extract, 35 mg protein; total volume 1.1 ml. Whole-cell reaction flasks contained: whole cells in their growth liquor, OD 0.58; total volume 1.0 ml. Each flask contained the appropriate pesticide in dimethylformamide, amounts as indicated. Gas atmosphere, $H_2 : CO_2$, 80 : 20. Temperature, 40° C.

The effect of DDT and some of its derivatives on CH_4 biosynthesis suggests that the inhibitory site is centred in the trichloroethane portion of the molecule. Removal of one chlorine (DDD) reduces inhibitory activity. Removal of two chlorines (DME) renders the molecule inactive as does modification of the ethane moiety by oxidation to a double bond (DDE), whereas removal of the ring chlorines and replacement with methoxy groups have very little effect. DDT has been reported to affect many enzymes or enzyme systems, but usually these effects have required extremely high concentrations of DDT or else have been duplicated by non-toxic analogues of DDT, and so discredited[9]. Just the opposite effect is observed in the methane biosynthetic system which is sensitive to low concentrations of DDT (10^{-6} M), and inhibition is observed only with DDT analogues which have pesticide activity. The CH_4 synthesizing system may be a good tool for studying the mechanism of DDT inhibition. The similarity between the active site of DDT and chloroform is evident, but it is not known whether they inhibit by the same method. $CHCl_3$ is thought to inhibit by alkylating B_{12} (ref. 4); DDT cannot alkylate B_{12} chemically; so it is unlikely that this reaction accounts for its inhibitory properties.

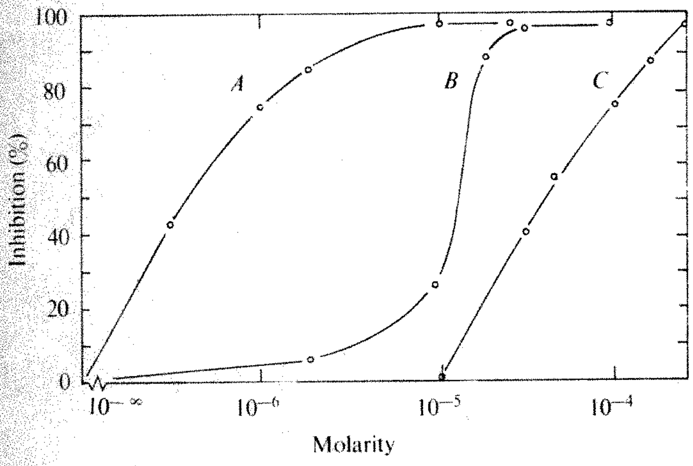

Fig. 1 *A*, Effect of DDT on methane biosynthesis in cell extracts of *Methanobacterium* strain M.o.H. Reaction mixtures contained: TES buffer [N-*tris*-(hydroxymethyl) methyl-2-aminoethane sulphonic acid], *p*H 7.0, 200 μmol; adenosine triphosphate, 10 μmol; DDT dissolved in dimethylformamide, amount as indicated; crude cell extract, 35 mg of protein. Total liquid volume 1.1 ml. Gas atmosphere 80% H_2 and 20% CO_2. Temperature 40° C. *B*, Effect of DDT on methane biosynthesis in whole cells of *Methanobacterium* strain M.o.H. Whole-cell reaction mixtures contained: DDT in dimethylformamide, amount as indicated; whole cells in growth liquor, absorbance 0.58. Total volume 1.0 ml. Gas phase was 80% H_2 and 20% CO_2. Incubation temperature 40° C. *C*, Effect of DDD on methane production in cell extracts of *Methanobacterium* strain M.o.H. Each reaction mixture contained: TES buffer [N-*tris*-hydroxymethyl) methyl-2-aminoethane sulphonic acid], *p*H 7.0, 200 μmol; adenosine triphosphate, 10 μmol; DDD in dimethylformamide, or dimethylformamide, amount as indicated; crude cell extract 35 mg of protein; gas atmosphere 80% H_2 and 20% CO_2. Total liquid volume 1.1 ml., temperature 40° C.

DDT has been shown to inhibit carbonic anhydrase activity in the shell gland of the Japanese quail[10]. The methanogenesis reaction also involves an activation of CO_2, and it would be interesting to determine if the latter inhibition is functioning by a similar mechanism.

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Patterns of Hormone Excretion in Male and Female Homosexuals

We have reported that urinary testosterone levels tend to be low in male homosexuals, while in lesbians high levels of testosterone and luteinizing hormone (LH) coincide with abnormally low values for oestrogen output[1]. The purpose of this communication is to extend this work by presenting a comparison of excretion patterns for these hormones with those of normal heterosexual men and women.

The heterosexual controls were chiefly members of the scientific and technical staff of the Clinical Endocrinology Unit. All were volunteers, none of whom admitted to homosexual inclination or activity. Urinary testosterone readings in the male controls (Figs. 1 and 2) were derived from the studies previously published from our unit[2,3]. With the female controls, urinary testosterone, oestrone and LH levels were those quoted in our earlier publications dealing with endocrine function in normally menstruating women[4,5].

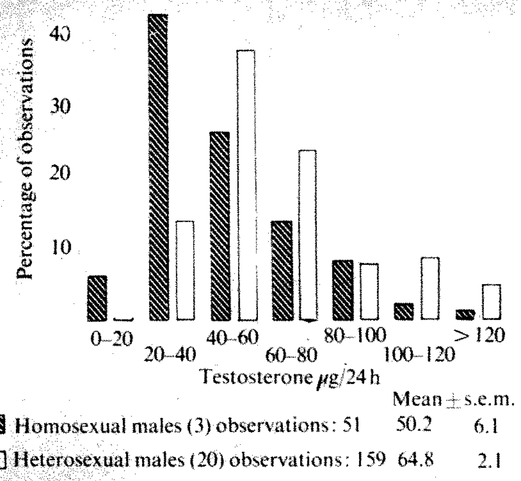


Fig. 1 Distribution of urinary testosterone values in normal heterosexual and homosexual males.

Three male and four female homosexuals were studied; detailed clinical information is published elsewhere[1]. The ages of the three men were respectively 19, 29 and 33 yr. All were healthy and ambulant and none received any form of medication during the period of investigation. The homosexual role adopted varied with each individual, being active and passive on different occasions. One of the subjects engaged in both homosexual and heterosexual activities. The duration of the investigation ranged from 19 to 26 days.

The four lesbians were two pairs of sexual partners; the ages of the first two were 23 and 20 and of the second 21 and 20. All were ambulant and engaged in very heavy sexual activities except at the time of menstruation; one of the women admitted to previous heterosexual experiences but had since become completely homosexual. Subjects 1, 2 and 4 had a past history of irregular menstrual cycles. Subjects 1, 2 and 3 had cycles lasting 30, 33 and 30 days respectively and all menstruated for the first 4 days of the investigation which ended on the first day of the next menstrual period. In subject 4, menstruation occurred during the last 5 days of the study which continued for 44 days. A tentative diagnosis of the Stein-Leventhal syndrome made in subject 4 was not confirmed at laparoscopy, both ovaries being of normal size.

Hormone assays were performed on 48 h pools of urine, results being expressed per 24 h sample. Great care was taken to ensure that complete urine collections were made. Techniques in routine use in this unit for testosterone[6], oestrone[7], pregnanediol[8] and LH[9] were used.

Fig. 1 shows the distribution of urinary testosterone readings in the three male homosexuals and in normal heterosexual controls. The incidence of low testosterone readings in the homosexual group is considerably greater than in the normal group. Some 6% of the values obtained from homosexuals lay between 0 and 20 μg/24 h as compared with none in the heterosexual males. More than 40% of the readings in the homosexuals were in the range 20 to 40 μg/24 h, compared with less than 15% in the heterosexual subjects.

The tendency for urinary testosterone readings to be low in male homosexuality is further demonstrated in Fig. 2, which compares results of serial assays in the homosexual and heterosexual groups. Thus in all three homosexual subjects levels tended to be at the lower end of or below the normal range for varying periods of time ranging between 5 and 14 days. In the one male (subject 3) who engaged in both homosexual and heterosexual activities, excretion values for urinary testosterone showed the greatest variation and rose to a marked peak equal to the highest point in the normal range, during the last 5 days of the investigation. In the two subjects who were exclusively homosexual in their orientation comparably high values were not observed.

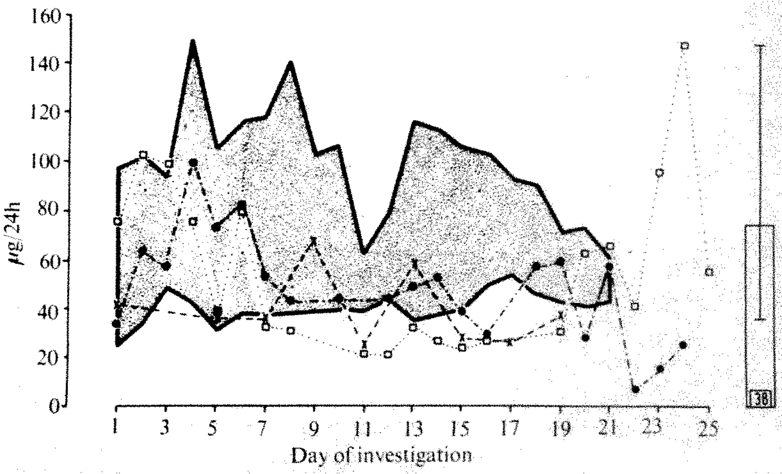
In Figs. 3, 4 and 5, excretion values for urinary testosterone, oestrone and LH in the four lesbians are shown, together with the range in heterosexual controls.

In the case of testosterone and oestrone excretion in normal subjects the reference point in the cycle—designated day 0—was the mid-cycle peak of oestrone oestradiol. For LH the reference point (day 0) was the mid-cycle peak of the hormone itself. In the first three female homosexuals the reference points were the peaks of oestrone/oestradiol occurring at or about mid-cycle, while in subject 4 the reference point was the highest LH value recorded.

Fig. 3 shows that urinary testosterone readings in female homosexuals are considerably higher than in heterosexual controls. Furthermore, the pattern of testosterone output differs from normality in all four subjects. Thus in subject 1, readings were high early in the cycle (days 1–4), rose to an exaggerated peak during the luteal phase (days 21–22) and then fell abruptly towards the end of the cycle. In subject 2, readings were again high early in the cycle (days 1–6) and showed marked peaks on days 15–16 and again on days 21–22. In subject 3, levels were grossly elevated initially, fell during the follicular phase and rose to a second peak on days 13 and 14; high levels persisted during the luteal phase. Subject 4 also showed high readings throughout the initial period of investigation, there being a series of four peaks during the first 23 days of the study succeeded by levels largely within the normal range but which rose again during menstruation at the end of the study.

The important point to note in Fig. 4 is that levels of oestrone tended to be lower in the homosexuals than in the heterosexual controls. In subject 1, a small peak of this steroid was detected at mid-cycle (days 15–16) and was followed by a well defined rise on days 21–26. Distortions of the pattern of oestrone excretion were observed in subjects 2, 3 and 4. In subject 2, peaks of excretion were detected towards the end of menstruation from days 3–6, at mid-cycle and again late in the cycle. A mid-cycle

Fig. 2 Testosterone excretion in normal heterosexual and homosexual men. The stippled area shows the normal range from ref. 2, and the open column shows the normal range from ref. 3. ×, Subject 1; ●, subject 2; □, subject 3.



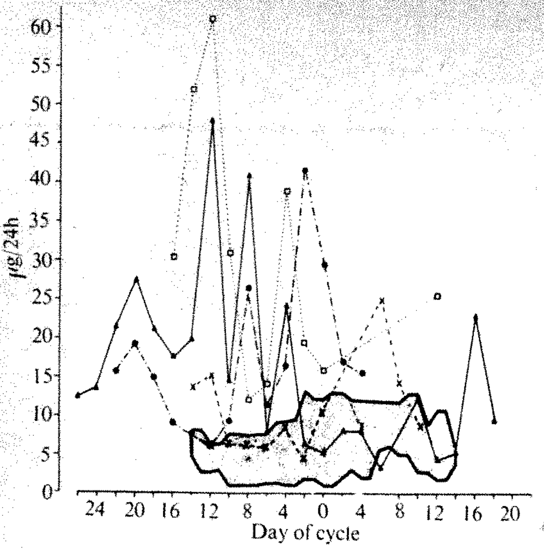


Fig. 3 Testosterone excretion in normal heterosexual and homosexual women. The stippled area shows the normal range from ref. 4. ×, Subject 1; ●, subject 2; □, subject 3; ▲, subject 4.

peak on days 17–18 was noted in subject 3, after which the steroid could not be detected during the rest of the cycle. A more extreme example is seen in subject 4 in whom oestrone was only detectable on 10 out of the 44 days of the study.

The most important findings illustrated in Fig. 5 are that urinary LH values tend to be considerably elevated in homosexuals and that pronounced distortions in the pattern of excretion of this hormone occur in this group. Although in subject 1 a peak of LH was only detected at mid-cycle, in subjects 2 and 3 gross irregularities in excretion values were observed with abnormally high readings on days 8–9, 22–23 and 28–29 in the former and on days 1–2 and 11–12 in the latter. In subject 4 two clearly defined peaks of LH were measured, one at the beginning of the study and one 16 days before menstruation commenced.

Urinary pregnanediol assays are a useful indication of luteal function and of the occurrence of ovulation. In subject 1, a rise in pregnanediol excretion to 2 mg/24 h occurred on days 19–20 of the cycle; in subject 2 two peaks were identified, one on days 4–5 (4.8 mg/24 h) and the other on days 32–33 (3.9 mg/24 h). The peak excretion in subject 3 (2.8 mg/24 h) was noted on days 15–16 and in subject 4 the maximal pregnanediol value (1.5 mg/24 h) was encountered four days before menstruation.

The striking feature of our study was the gross distortion of the pattern of testosterone, oestrone and LH output in the four female homosexuals, which occurred irrespective of whether the role adopted in sexual activities was active or passive. In one of the lesbians ovulation definitely took place; in two subjects evidence for ovulation was equivocal and in the remaining woman it was absent. In the male homosexuals deviations from normality in terms of endocrine function were much less marked than in the females.

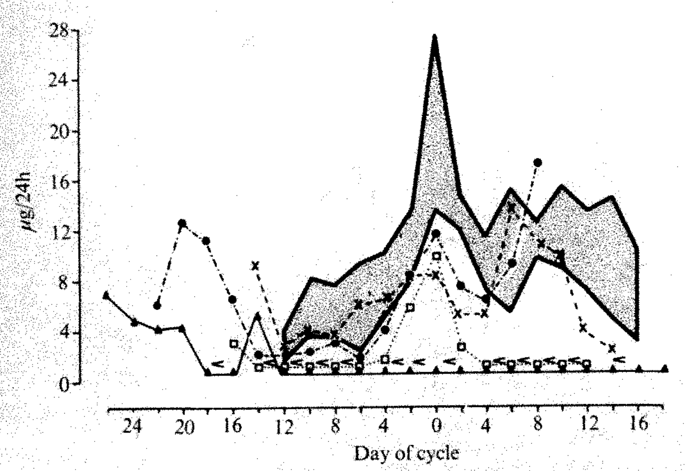


Fig. 4 Oestrone excretion in normal heterosexual and homosexual women (notation as in Fig. 3).

Previous studies of endocrine function in homosexuality have been sparse, largely because traditionally the condition has been regarded as psychogenic. More recently, however, it has been suggested that the aetiology of homosexuality may be multifactorial[10]. Endocrine factors are implicated in human subjects both by our data and by the observation of Margolese[11] that the ratio of androsterone to aetiocholanolone differs between male homosexuals and their heterosexual counterparts.

The precise cause of the endocrine imbalance in homosexuality remains to be established. Obviously such abnormalities could stem from the impingement of psychological factors on hypothalamic centres. Alternatively a hormonal imbalance occurring during periods of life at which the direction of future sexual behaviour is determined could play a role, and there is now extensive work in various animal species to support this viewpoint[12–14].

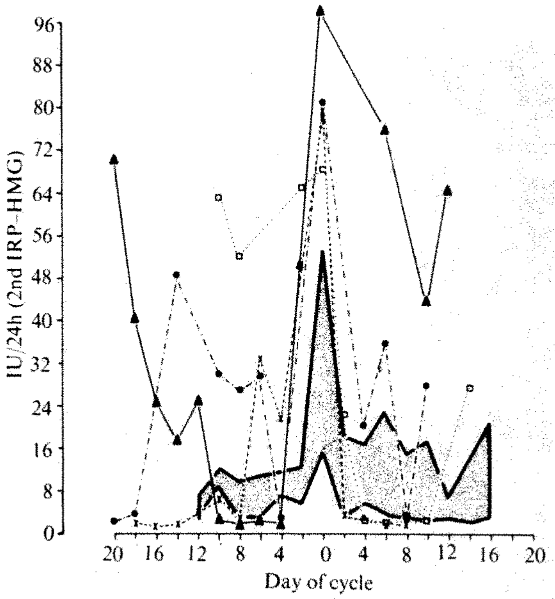


Fig. 5 LH excretion in normal heterosexual and homosexual women. The stippled area shows the normal range from ref. 5 (other notation as in Fig. 3).

Abnormalities of endocrine function have recently been demonstrated in other conditions which have formerly been regarded as psychogenic, for example, incapacitating dysmenorrhoea in women[15] and impotence in men[3]. People suffering such forms of hormonal imbalance are tolerated without question by society, and if the results of our investigations are confirmed a reappraisal of social attitudes to homosexuality might become necessary.

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Coital Rates and the Pill

Udry and Morris[1] suggested that oral contraceptives abolish the depression in coital rates characteristic of the second half of the menstrual cycle in women not using these drugs. They speculate that this may be due to the absence (because ovulation has been suppressed) of a luteal surge of progesterone. I should like to comment first on this putative explanation and second on the support given by Udry and Morris's data for their contention.

Unquestionably the administration of androgens increases libido in some women: but libido in the human female is not solely dependent on reproductive secretions[2]. So to what extent are coital rates affected by fluctuations in female hormone levels occurring naturally or as a consequence of the ingestion of oral contraceptive pills?

Udry and Morris[3] have suggested that within the intermenstruum the distribution of coitus of women not using oral contraceptives is subject to cyclic fluctuations associated with their endogenous hormone levels. They claim that the maximum coital rate occurs in the middle of the cycle roughly at the time of ovulation, and that the rate declines thereafter. I have re-analysed their raw data, those of McCance *et al.*[4], and some raw data of my own, and have reached another conclusion[5]. With this more extensive material, I only pooled cycles with others of the same length (thus avoiding the necessity for standardizing for length and for using a reverse time scale). Moreover, I took account of the fact that some couples practise coitus during the menses while others do not.

The results clearly indicate that the highest coital rates in the intermenstruum (using that term to denote days on which there is no bleeding) occur immediately after menstruation has ceased—not at ovulation time, but well before. The rate then steadily declines throughout the intermenstruum and there is little evidence for any increase associated with ovulation.

It seems to me that a major cause of this high coital rate after the cessation of menses is probably the abstinence which most couples exercise during all or part of the menses. The point could be tested by examining the coital records of couples who are indifferent to such niceties: if I am right, their coital rates would not show this decline through the intermenstruum. Such data would indicate whether coital rates are associated at all with the cyclic fluctuations of female hormone levels.

It seems possible that women using oral steroid contraceptives have higher rates than other women when age, race, education and religion are controlled[6], though it should be noted that these controls were not simultaneous. In this study the data did not support the suggestion that women who choose to use the pill are women who in any case have higher coital rates (though in my opinion this point needs further testing). On the average, the coital rates of women on the pill increased over a period of time, while the rates of a control group declined. In another study the coital rates of women on the pill remained roughly constant with time[17]. In yet another study there was no significant difference between the coital rates of women who did, and women who did not, use the pill[1].

Other workers have found that after women start using an oral contraceptive, more of them report an increase than a decrease in coital rates[7], libido[8–13] or both[14,15]. None of these studies offers evidence that this effect is due to the active ingredients of the pill rather than to the psychological consequences of abandoning a messy or inefficient system of birth limitation. The results of other workers suggest that women suffer no real change in libido[16], or that libido increased in some women and decreased in others to about the same extent[17]. One study suggests that more women suffer a decrease than an increase[26]. Other workers have suggested that women on the pill suffer a decline in libido[18–25]. Of these latter studies, however, three[21–23] were based wholly or partly on reports of women who previously had had untoward side effects with an oral contraceptive; none reported the number of women claiming an increase in libido; and only one[20] incorporated a control group taking placebos and thus was capable of distinguishing the direct effect of the drug from the psychological sequelae attendant on its known contraceptive properties. This study, however, was arguably conducted on samples that were too small (ten in the control and ten in the experimental groups) and for too short a time.

It has been suggested that among women using oral contraceptives, a small proportion are very depressed[27–29]. It is not known whether the drug causes this depression[30], but it is at least possible. One might suppose that there is a considerable overlap between this small group and women whose coital rates are reported to decline when they use the pill. So I would be inclined to suppose that oral contraceptives are associated with two opposing (and roughly equal) effects on coital rate. First, in a small proportion of women the coital rate declines, very possibly as a direct pharmacological consequence. Second, in another proportion of women (probably larger) the coital rate increases as a psychological consequence of using a reliable form of birth limitation.

However, one would suppose that women of the former group are more likely to abandon the pill than women in the latter group. Hence the overall effect of the pill on coital rates would be, presumably, to increase them.

Among those claiming that libido diminishes in women taking oral contraceptives, some authors have suggested that this diminution is more associated with strongly progestogenic drugs than with strongly oestrogenic ones[18,19]. Other data have failed to support this finding[24].

In short, it is by no means clear whether libido is increased or decreased in most women using these drugs. *A fortiori*, it is not known whether any changes in coital rates occur as a direct result of these drugs. *A fortiori*, the suggestion that there is a decrease in coital rates, and that this is due to the progestogenic component of those drugs, is to be regarded with reserve.

Marital coital rates are not closely associated with female hormone levels (occurring either naturally or as a result of contraceptive pills): certainly not as closely as Udry and Morris supposed.

I am in any case doubtful of the phenomenon that Udry and Morris were explaining. To see whether the ingestion of a drug alters the time trend of coital rate within the menstrual cycle, it is appropriate to test the significance of the difference between the regression coefficients of the rate (with and without drug) on cycle day. In the data I have examined, there is no clear suggestion that the trend is not linear with time after menstruation has ceased: it seems reasonable to assume that none of the women in Udry and Morris's sample was menstruating after the seventh standardized cycle day. So one can test the significance of the difference between the linear regression coefficients of coital rate on cycle day for the time period day 8 to day 28 inclusive for Udry and Morris's two samples (those taking and those not taking oral contraceptive drugs). For this test, $t=0.8$, $0.5>P>0.4$. So Udry and Morris's data provide little support for their contention that the pill abolishes the decline in coital rates during the second half of the cycle.

It seems to me that endocrinologists might find it more rewarding to investigate the association between fluctuating male hormone levels and human coital rates[31]. After all, it has been suggested that the husband has more say than the wife about the occurrence of marital coitus[32,33].

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Electrical Activity of Oviducts *in vivo*

There have been few attempts directly to measure the electrical activity of oviducts *in vivo*, although excised tissues have been studied, in continuation of earlier observations of oviductal movements or ciliary action[1–4]. We now wish to report direct observations of electrical activity made in twenty intact goats over periods of months. Special platinum electrodes in plastic collars were implanted surgically, with the leads passing to the exterior. We experienced no problems with infection.

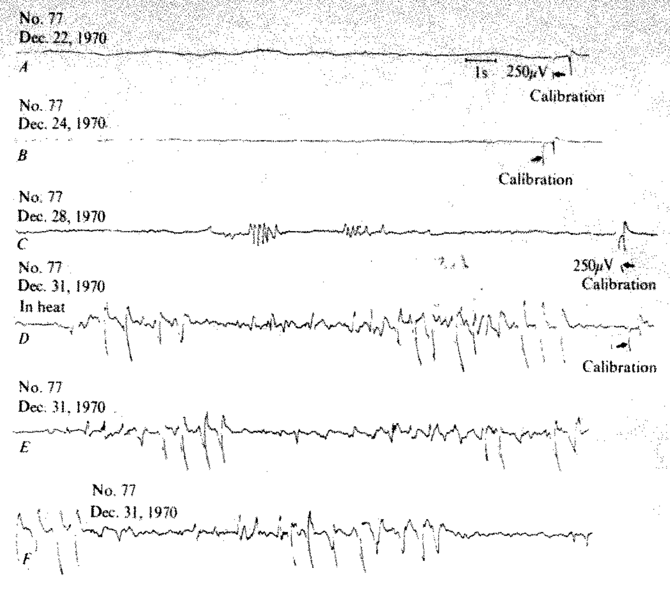

Fig. 1 Evolution of the bioelectric activity of the oviducts from the epoch before oestrus to the oestrous period. *D*, *E* and *F*, characteristic oestrous activity.

Figs. 1 and 2 show the typical patterns of electrical activity, with electrodes on the isthmus and infundibular areas of the oviduct in the non-pregnant animal. Fig. 1 shows that initial recordings on tracings *A* and *B* are quiet, demonstrating little activity. Tracing *C* shows trains of positive pulses, about 125 μV in amplitude. With the animal in oestrus, tracings *D*, *E* and *F* show pronounced electrical activity. In the most consistent pattern, groups of 250 μV positive pulses (upward in our system) are followed by large negative pulses in groups or trains, with amplitudes up to 600 μV.

This oestrous pattern was followed by a changed pattern 2 days later, in which negative pulses alone were dominant (Fig. 2, tracing *A*), with the epoch now corresponding to the time of ovum transport. Oestrus was determined by vulval

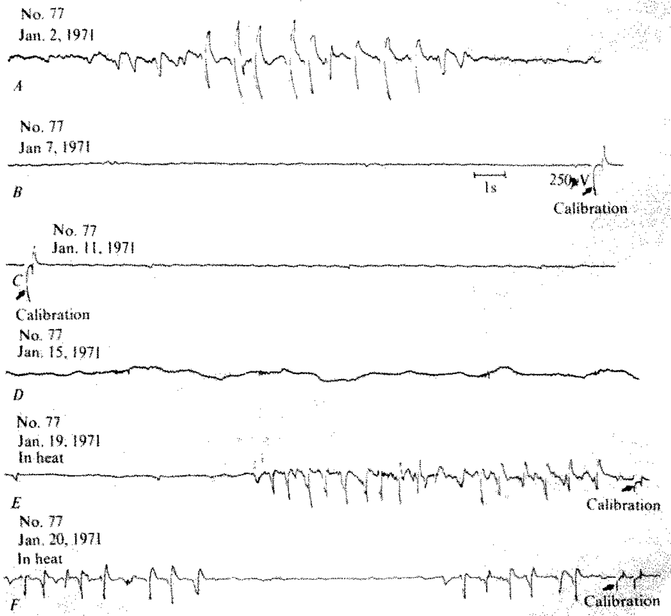

Fig. 2 *A* shows a changed pattern, showing that negative pulses predominated at a time of presumed ovum transport. The activity of tracings *B*, *C* and *D* may be contrasted with the reappearance of bursts of large pulses in the next heat, *E* and *F*.

swelling, some discharge, excitability, tail held high and powerful response to the presence of a teaser male.

Fig. 2 shows that the electrical activity in succeeding days decreases to a very low value, with only the presence of infrequent, small characteristic pulses. With the approach of the next oestrus, there was an increase in slow wave activity, and then with the animal in the second recorded oestrus, pronounced trains of electrical activity reappeared.

Further investigations of the directions of propagation and the presence of pacemaker function are certainly indicated. It has not escaped our notice that the demonstration of this electrical activity and concomitant increased comprehension of oviductal function may lead to the development of new methods of contraception.

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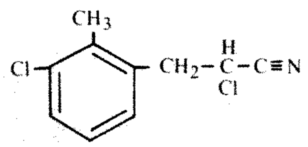
α-Chloro-β-(3-Chloro-*o*-Tolyl) Propionitrile, a New Synthetic Auxin

IN several field and some laboratory experiments it was recently found that α-chloro-β(3-chloro-*o*-tolyl)propionitrile (PRB-8) stimulates vegetative growth in several cultivated plant species[1].



This compound and some other derivatives were put at our disposal for further research. Purity of the compound was 100% as controlled by TLC. PRB-8 seemed to exert a remarkable growth promoting activity in generally applied tests for auxins. Table 1 shows some results of representative experiments with segments of coleoptiles of *Avena sativa*[2] and of hypocotyls of *Phaseolus aureus*[3]. Some other "auxins" are included in these tests for comparison. It was not possible to test higher concentrations because of the low water solubility of PRB-8 (about 10 p.p.m. at 25° C).

From these and many other experiments it may be concluded that PRB-8 behaves as other known auxins or as the auxin-herbicide 2-4 D. But PRB-8 seemed to have more characteristics of a true auxin than of an auxin-herbicide. Indeed, seed germination tests[4] (also on filter paper) indicated that straight growth of roots could be enhanced (at a concentration of ±0.001 p.p.m.). Furthermore, in comparison with other "auxins" PRB-8 demonstrated a greater stimulating effect and a smaller inhibiting effect at concentrations greater than 0.01 p.p.m. The results obtained with seeds of *Raphanus sativus* L. (red radish) are represented in Fig. 1. Similar results are observed with seeds of other plants (for example, *Brassica oleracea* L. cultivar, curled cabbage, *Lepidium sativum*, and *Cichorium endivia* L.). In some trials the growth stimulating effect was less evident on these plants than on radish.

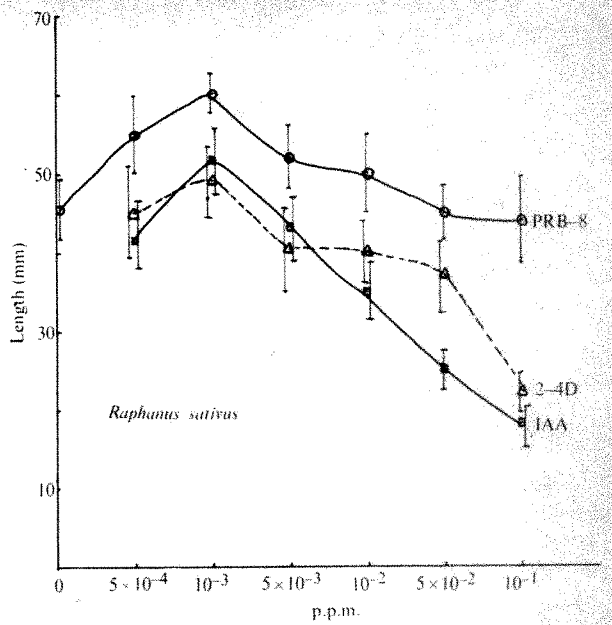


Fig. 1 Length of the roots, 3 days after germination on filter-paper saturated with a solution of the growth regulator at the appropriate concentration. Temperature: 22° C. The values are the mean of fifty roots.

Table 1 Increase in Length as % of Control Elongation Growth of Segments (0.5 cm) from Mung Bean Hypocotyls and *Avena* Coleoptiles, Measured after 18 h

	Phaseolus			*Avena*						
	Concentration (p.p.m.)									
Auxin	10	5	1	10	5	1	0.5	0.1	0.05	0.01
IAA	206	193	187	211	211	188	188	177	172	111
IAN	143	187	175	—	—	—	—	—	—	—
NAA	193	206	200	270	270	280	260	200	220	100
2–4 D	200	206	137	270	280	300	290	210	170	110
PRB-8	231	250	206	210	240	180	160	130	120	100

IAA, Indolylacetic acid; IAN, indolylacetonitrile; NAA, α-naphthylacetic acid; 2-4 D, 2-4-dichlorophenoxyacetic acid.

Root-elongation-growth is inhibited at concentrations greater than 1 p.p.m., but these concentrations caused a thickening of the root associated with the formation of a large number of lateral primordia. This phenomenon is also known for other growth-regulators. Otherwise, up to a concentration of 10 p.p.m., inhibition of seed germination was never observed. IAA in these experiments had an additive effect; there is no known interconversion between IAA and PRB-8.

As could be expected, PRB-8 exhibits auxin activity also in other physiological processes. Preliminary experiments show that 1 and 10 p.p.m. PRB-8 delays abscission of debladed petioles of Coleus and that 10 p.p.m. PRB-8 also stimulated the formation of adventitious roots in cuttings of this plant species.

We have also investigated the relationship between the chemical structure of this type of compound and its biological activity. We found that the presence of Cl in the side chain

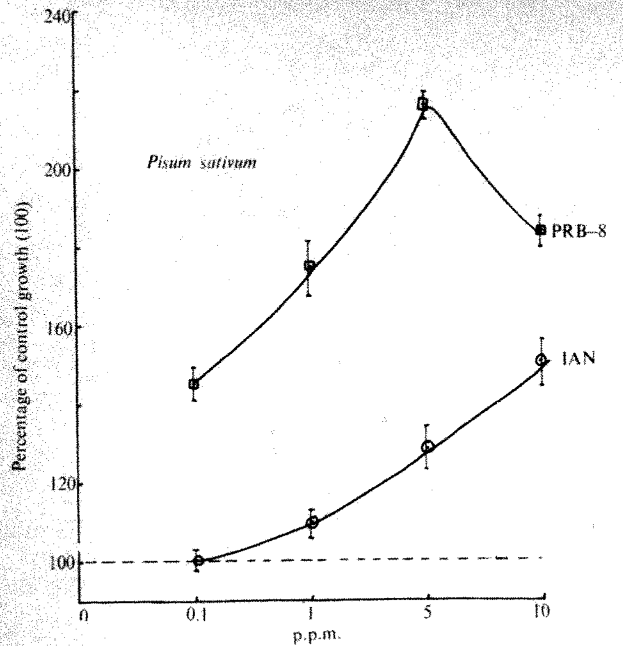


Fig. 2 Elongation growth of segments of *Pisum* shoots (0.5 cm) in the presence of PRB-8 or IAN (indolylacetonitrile). Values are the mean of twenty segments.

is essential for biological activity. Substitution of Cl at the 4, 5 or 6 position in *o*-tolyl always gave physiologically inactive compounds.

Generally, growth regulators with an acetic acid side chain (IAA, 2-4 D) are as active as their corresponding nitriles (except in tissues of some plants, for example, *Pisum sativum*). An interesting feature of the work of Fawcett *et al.*[5] was that acids or nitriles with an even number of side chain methylene groups yielded acetic acid by repeated β-oxidation in wheat tissues. The physiological activity of the nitriles was explained by hydrolysis of —CN to —COOH, followed by β-oxidation. ω-2-4-Dichlorophenoxy-propionic-acid is inactive, however, while the nitrile is only very slightly active. This behaviour could be due to an α-oxidation ($—CH_2CN \rightarrow —COOH$[5]).

With these results in mind, the activity of PRB-8 is interesting in comparison with IAN (indolyl acetonitrile) in segments of *Pisum* and mung beans (Figs. 2 and 3). In *Pisum* as in mung bean segments, PRB-8 is much more active than IAN.

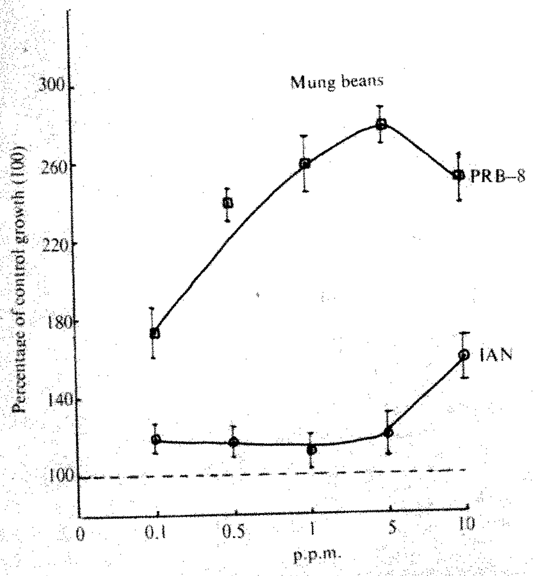


Fig. 3 Elongation growth of segments from mung bean hypocotyls in the presence of PRB-8 or IAN (indolylacetonitrile). Values are the mean of twenty segments.

On the other hand, if the nitrile function of PRB-8 is replaced by —COOH (α-chloro-β(3-chloro-*o*-tolyl)propionic acid) no growth promoting activity is detected in growth tests with segments of *Avena* and mung beans. The same is true if the acid is dissolved at *p*H 3–8 or is applied as the sodium salt.

Table 2 Root and Shoot Growth in a Germination Test with Seeds of *Raphanus sativus*[5]

	PRB-8 (nitrile)				PRB-8 (acid)			
	Shoot		Root		Shoot		Root	
p.p.m.	mm	%	mm	%	mm	%	mm	%
0	5.5±0.8	100	25.3±4.2	100	5.5±0.8	100	25.3±4.2	100
0.1	2.7±0.4	49	8.1±1.5	31	7.6±1.3	138	37.2±3.6	147
0.05	7.4±1.8	134	30.1±2.1	118	8.5±1.1	154	36.3±3.5	143
0.01	—	—	—	—	8.0±1.2	145	27.9±3.1	110
0.005	8.8±1.2	160	34.1±2.6	134	5.7±0.9	104	26.7±3.3	105
0.001	7.2±1.3	130	31.6±2.7	124	7.3±1.4	132	30.7±3.5	121

Seedlings were germinated for 3 days at 22° C. The values are the mean of twenty seedlings.

Nevertheless, the acid is physiologically active in germination tests with seeds of red radish. Concentrations greater than 1 p.p.m. are inhibitory while other concentrations enhance shoot and root elongation growth (Table 2). The acid is also inactive in the abscission test and does not induce adventitious roots in cuttings of different plants.

Because of these results, it seems worthwhile to study PRB-8 in more detail. Work is in progress concerning the metabolism and transport characteristics of ^{14}C-labelled PRB-8.

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Effects of Cyclophosphamide on Serum Immunoglobulin Levels in SJL/J Mice

Hypergammaglobulinaemia is common in SJL/J mice[1,2], an inbred strain which develops spontaneously a high incidence of lymphoma[3] and amyloidosis[4]. A number of the immunoglobulin elevations are electrophoretically indistinguishable from the "M" proteins seen in multiple myeloma[1], but most are broadly dispersed electrophoretically and involve a single immunoglobulin fraction with elevations occurring as early as 6 weeks of age[4]. Less frequently, two and occasionally three or more fractions are increased[5,6].

Evidence for tumour specific antigens in SJL/J mice has come from studies of the transplantation behaviour of SJL/J lymphoma and of the capacity of certain tumour-sensitized spleen cells to protect recipients transplanted with syngeneic tumour grafts[7–9]. In addition, we have obtained evidence in support of the idea that hypergammaglobulinaemia represents an immunological host response to tumour-associated antigen(s)[6,9]. In an attempt to change this host response, we first examined the effects of cyclophosphamide, given for up to 6 months, on the serum levels of individual immunoglobulin fractions, γ_1, γ_{2a}, γ_{2b}, IgA and IgM[10–12] in male SJL/J mice. This drug is a powerful immunosuppressive agent[13] when given in relatively non-toxic doses[14] and has been shown to strongly inhibit the ability of rodents to produce antibody after allograft transplants[15] and conventional antigens[16]. The immunoglobulin levels in untreated (colony) male SJL/J mice at all ages studied, were also measured to determine the immunoglobulin pattern and frequency and types of immunoglobulin elevations present in this population.

Male SLJ/J mice 6–10 weeks old, from the Jackson Laboratory, Bar Harbour, or bred at Rochester were divided into three groups and injected intraperitoneally with 12.5, 50 and 100 mg/kg of cyclophosphamide diluted with sterile saline to the appropriate concentration (mg/ml.). Controls were injected with sterile saline only. For the first three weeks the animals received three injections per week, in the fourth week two injections and from the fifth to 24th week one injection per week. Individual mouse immunoglobulin fractions were measured at the time of death in half of each group after 3 and 6 months[17]. Mice were weighed every second week and the dose of drug was adjusted on a mg/kg basis with changing total body weight. Blood obtained by tail vein bleeds or cardiac puncture after death was collected in microcapillary tubes and allowed to clot. The serum was separated after centrifugation and stored at −20° C. Control immunoglobulin levels were defined as the mean ±1 standard deviation (±s.d.) of the serum levels of individual immunoglobulin fractions obtained from untreated, non-tumour-bearing male SJL/J mice, 10–19 weeks of age. Serum values greater than the defined upper limits for each immunoglobulin class were considered hyperglobulinaemic.

The mean serum levels for individual immunoglobulin fractions in untreated male SJL/J mice are shown in Fig. 1. Hypergammaglobulinaemia was found in fifty out of ninety-three animals. The frequency of hyperglobulinaemia increased with age to reach 93% at 40–59 weeks but it fell to 75% after 60 weeks (Table 1). A hundred instances of individual immunoglobulin increases occurred in the fifty hypergammaglobulinaemic mice (Table 2). Increases involved all five fractions but chiefly γ_1 and γ_{2a} (Table 3). In twenty-eight animals, hyperglobulinaemia occurred with more than one fraction. Similar observations were made when a large colony of male and female SJL/J mice were combined (Hill, R. S., and Bakemeier, R. F., unpublished data).

The effects of prolonged cyclophosphamide administration on the serum levels of individual SJL/J mouse immunoglobulins are summarized in Table 4. After 3 months there was a marked dose-related suppression of γ_1, γ_{2b} and IgA fractions. Three of the five animals in the 100 mg/kg drug group also had strongly suppressed IgM serum levels of 0.03 mg/ml. (control 0.22 ±0.11 mg/ml.) but the remaining two had elevated IgM levels. The levels of γ_{2a} did not differ significantly from the control levels. The two IgM elevations in this high dose group (two of fifteen treated animals) were the only cases of hyperglobulinaemia found in the treated animals at 3 months of age.

Table 1 Age Related Incidence of Hypergammaglobulinaemia in Male SJL/J Mice

Age (weeks)	Total No. of animals	No. with elevations	% Incidence
0–19	35	10	29
20–39	32	18	56
40–59	14	13	93
60+	12	9	75

Table 2 Frequency of Hypergammaglobulinaemia in Male SJL/J Mice

No. of immunoglobulin fractions elevated*	No. of animals
1	22
2	15
3	5
4	7
5	1
	Total 50

* Greater than control levels. Controls: mean ± s.d. of untreated non-tumour bearing male SJL/J mice, 10–19 weeks old (γ_1 1.48 ±0.94; γ_{2a} 3.0±1.448; γ_{2b} 0.59±0.27; IgA 0.51±0.28; IgM 0.28 ±0.11 mg/ml.).

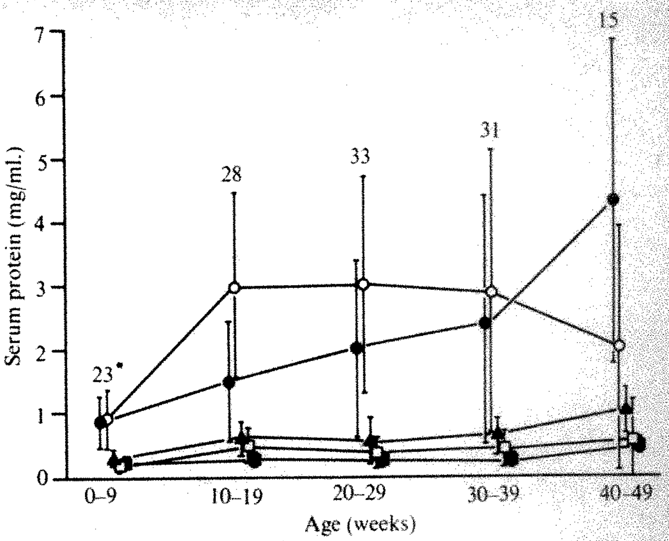

Fig. 1 Age-related serum immunoglobulin levels in male SJL/J mice. * Number of mice quantitated in each age group. Immunoglobulin classes: ●, γ_1; ○, γ_{2a}; ▲, γ_{2b}; □, IgA; ■, IgM.

Table 3 Frequency of Individual Immunoglobulin Fraction Elevations in Male SJL/J Mice*

Immunoglobulin class	Number of animals with single elevation	Total instances of hypergamma-globulinaemia
γ_1	6	23
γ_{2a}	6	27
γ_{2b}	1	16
IgA	2	15
IgM	7	19
	Total 22	Total 100

* 100 instances of individual immunoglobulin elevation, occurring in fifty hypergammaglobulinaemic mice.

After 6 months of treatment, none of the high dose (100 mg/kg) group was alive. Mice treated with 50 mg/kg continued to show γ_1 suppression, but no significant difference in the mean serum levels of other individual immunoglobulin fractions was found between control and treated groups at 6 months. All three surviving mice in the 50 mg/kg group had elevations of one or more of the immunoglobulin classes. One showed a γ_{2a} and a second an IgM increase; in a third, there was an increase in three fractions (γ_{2a}, IgA and IgM). In the 12.5 mg/kg group, two of five animals had increases, one involving γ_{2a} and a second IgM. Thus, in spite of 6 months of intermittent high dose cyclophosphamide administration, five of eight treated mice had developed hypergammaglobulinaemia, a frequency similar to that found in untreated animals of equivalent age.

The absence of tumours in animals from all cyclophosphamide-treated groups contrasts with the effects of repeated injections of antilymphocyte serum which causes the earlier development and faster growth of lymphoma in treated animals[18,19].

From these studies interesting differences were also found between γ_{2a} and other immunoglobulin classes in untreated mice when age-related serum levels were compared (Fig. 1). Thus,

Table 4 Effect of Cyclophosphamide on Serum Gammaglobulin Levels in Male SJL/J Mice

Cyclophosphamide dose (mg/ml.)	No. of animals	Immunoglobulin (fractions)* γ_1	γ_{2a}	γ_{2b}	IgA	IgM
3 months						
0	5	1.0 ±0.2	1.45±0.35	0.39±0.04	0.27±0.04	0.22±0.11
12½	5	0.98±0.27	1.74±0.74	0.37±0.08	0.21±0.04	0.14±0.04
50	5	0.25±0.55	1.3 ±0.4	0.27±0.14	0.21±0.08	0.15±0.03
100	5	0.2 ±0.3	1.4 ±0.62	0.037±0.01	0.05±0.03	0.8 ±1.37†
6 months						
0	5	1.35±0.61	2.07±0.52	0.41±0.17	0.28±0.04	0.33±0.23
12½	5	0.99±0.39	3.12±2.02	0.44±0.12	0.28±0.06	0.28±0.13
50	5	0.15±0.03	3.93±3.19	0.30±0.35	0.60±0.31	0.14±0.14

* Values expressed in mg/ml. ±s.d.
† Three of five animals < 0.03 mg/ml.

P values (3 months)
100 mg/kg: controls
100 mg/kg: 12.5 mg/kg
100 mg/kg: 50 mg/kg
} $P=0.05$ for γ_1, γ_{2b} and IgA

P values (6 months)
50 mg/kg: 12.5 mg/kg
50 mg/kg: control
} $P=0.05$ for γ_1

serum levels of γ_{2b}, IgA and IgM change very little in the first five decades. γ_1 levels rise more rapidly, approximately in parallel with the tumour incidence. Mean γ_{2a} levels tend to reach a peak by the end of the second decade and appear to fall during the period of high tumour incidence at 40–50 weeks (Fig. 1). The differences reported here between γ_{2a} and other immunoglobulin classes in the SJL/J mouse are in agreement with other findings of biological differences between γ_{2a} and other immunoglobulins in the SJL/J mouse[6,12]. The accumulating evidence suggests a possible immunological role for this protein in the pathogenesis of the spontaneous SJL/J lymphoma.

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Mitochondrial DNA of Human–Mouse Cell Hybrids

SOMATIC cell hybridization has revealed important facts about gene activity, differentiation and expression of genetic information in cells[1]. Eliceiri and Green[2] investigated the production of 28S ribosomal RNA in human–mouse hybrid cells and could detect only mouse ribosomal RNA. In a more recent study, however, Stanners, Eliceiri and Green[3] showed that hamster–mouse hybrids synthesized both hamster and mouse ribosomal RNA.

We have examined the mitochondrial DNA (M-DNA) from six human–mouse hybrid cell lines. From the experiments of Sarkissian[4,5] and others on maize hybrids, it was anticipated that interspecies hybrid cells might contain both types of parental mitochondria and M-DNA. The hybrid cell lines we have examined reflect a spectrum of established somatic cell hybrids and contained, at the time of analysis, possibly up to twenty human chromosomes.

Human and mouse M-DNA have buoyant densities in neutral CsCl of 1.700 and 1.692, respectively[6]. Equimolar mixtures of these two DNAs are thus easily resolvable in such gradients. The results of a series of experiments in which increasing amounts of M-DNA from the established human cell line HeLa were mixed with a constant amount of mouse L cell M-DNA and centrifuged to equilibrium (Fig. 1) illustrate that it is possible to detect less than 2% human M-DNA in a mixture containing approximately 1 µg of total DNA, an amount comparable to the yield of purified closed circular M-DNA obtained from the human–mouse hybrid cells for the analysis described.

The human–mouse hybrids used (Table 1 and Fig. 2) were obtained from a variety of crosses in different laboratories. Lines 4.12-Z and 4.43-Z come from a cross of a subclone of a 5BUDR resistant 3T3 subline (isolated by Howard Green) with human lymphocytes and were shown to express at the time of analysis respectively eleven and five unselected human enzyme markers out of the thirteen for which they were tested (two of which are linked)[7]. The mouse parent line in this cross does not contain any biarmed chromosomes and the mean number of biarmed chromosomes, presumably of human origin, 4.12-Z and 4.43-Z is eleven and eight respectively. Lines 3W4 and 4W10 are derived from a cross of human lymphocytes with an 8-azaguanine resistant L cell derivative[10,11].

A rough karyotypic analysis, based on gross chromosome morphology, suggested that the cells used for making mitochondrial DNA preparations from these two hybrids contained a minimum of five to ten human chromosomes. These lines both expressed human LDH A and B and indophenol oxidase and reacted strongly to a nonspecific rabbit anti-human serum[10,11]. The HLE-C hybrid was obtained from a cross of HeLa with a 5BUDR resistant 3T3 derivative[12]. This line contained originally more than thirty presumptive human chromosomes, but at the time of analysis this number had decreased to a mean of seventeen. The last hybrid results from a cross of Littlefield's 8-azaguanine resistant L cell derivative, A9, with Daudi, a human lymphoma cell line[13]. This contained about eighteen biarmed presumptive human chromosomes at the time of our analysis.

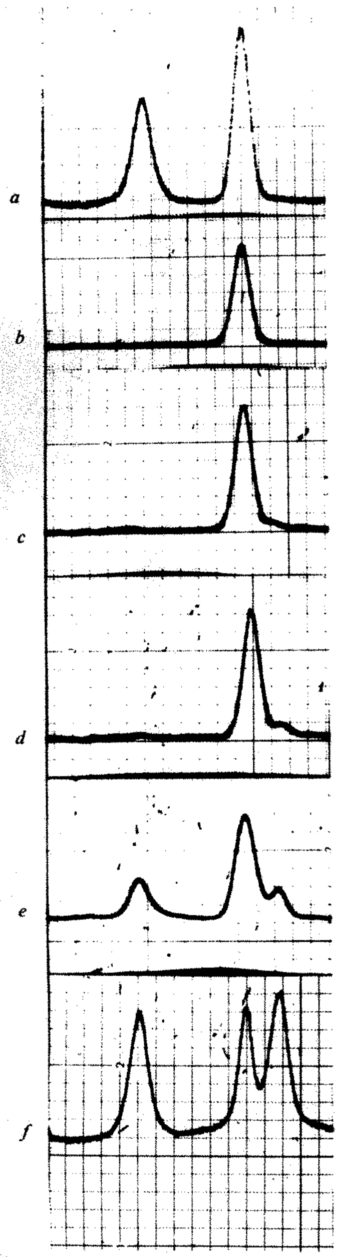

Fig. 1 Photoelectric scanner traces of synthetic mixtures of mouse and human M-DNA in neutral buoyant CsCl at 25° C, 44k r.p.m. 0.01 M Tris (pH 7.2); $\mathcal{S}=1.695$ CsCl in the Beckman model E ultracentrifuge. The density gradient is from left to right. *a*, Mouse L cell M-DNA against crab dAT marker. The mouse M-DNA bands at $\mathcal{S}=1.692$. *b*, Mouse L cell M-DNA. A synthetic series of mouse and human (HeLa) M-DNA was obtained by adding a known amount of human M-DNA to this mouse M-DNA sample. *c*, Mouse M-DNA (98.5%) plus human M-DNA (1.5%). The human M-DNA is indicated by a shoulder on the dense side of the band. *d*, Mouse M-DNA (95%) plus human M-DNA (5%). The human M-DNA now forms a very pronounced dense shoulder. *e*, Mouse M-DNA plus human M-DNA with a crab dAT marker. The dense split band contains 88% mouse M-DNA and 12% human M-DNA. The densest band is human M-DNA. *f*, Mouse M-DNA plus human M-DNA with a crab dAT marker. The dense split band contains 45% mouse M-DNA and 55% human M-DNA. The buoyant densities of the two peaks are 1.692 and 1.700, respectively. Optical amounts of stock DNA were used to enable us to calculate the amounts added for each experiment. The samples were checked by running separate buoyant analyses on a duplicate human aliquot to calculate the actual amount added and monitor the peak size of each human M-DNA sample alone. These two stock DNAs were found to contain less than 1% linear forms by electron microscopy[7].

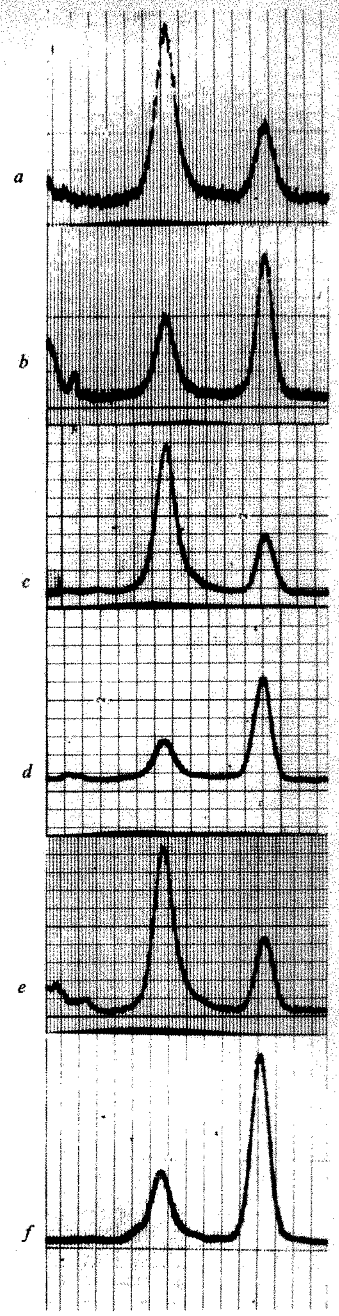

Fig. 2 Buoyant analyses of hybrid cell M-DNA at the centrifuge conditions described in Fig. 1. *a*, M-DNA from 4.12-Z against crab dAT. *b*, M-DNA from 4.43-Z against crab dAT. *c*, M-DNA from 3W4 against crab dAT. *d*, M-DNA from 4W10 vs. crab dAT. *e*, M-DNA from HLE-C vs. crab dAT. *f*, M-DNA from A9/Daudi against crab dAT. In each case the light band is crab dAT and the heavy band is hybrid cell M-DNA. In no case was there any evidence for any DNA banding as a dense shoulder or peak relative to the main band mouse M-DNA, even in traces expanded on an X-Y recorder[7]. Electron microscope analyses of each fraction revealed forms consistent with that for mouse M-DNA[6,9] and less than 2% linear forms. In each case, the mouse M-DNA displayed a gaussian distribution with a peak at $\mathcal{S}=1.692$. Human M-DNA has a buoyant density of 1.700[6].

Density gradients of mitochondrial DNA preparations from these six hybrids are shown in Fig. 2. There is no detectable nucleic acid at the position expected for human M-DNA in any of these analyses, suggesting that the M-DNA is, in each case, entirely of mouse origin. Electron microscopic examination of each of the M-DNA samples showed that more than 98% of the DNA present was circular and of a form consistent with

Table 1 Hybrid Cell Lines

Hybrid line	Human parental line	Mouse parental line	Generations after hybridization	No. of human chromosomes present
4.12-Z	Normal lymphocyte	1-T (3T3 deriv.)	12	11+
4.43-Z	Normal lymphocyte	1-T (3T3 deriv.)	8	8+
3W4	Normal lymphocyte	1-R (L fibroblast)	21	7–10
4W10	Normal lymphocyte	1-R (L fibroblast)	15	3–16
HLE-C	HeLa	3T3 (TK⁻)	—	17+
A9/Daudi	Daudi human lymphoma	A9 (L-fibroblast)	—	—

Six hybrid lines were examined. M-DNA was isolated at the generation noted above by methods previously reported[4]. The number of human chromosomes was determined from karyotypes prepared at the time of M-DNA analysis. Decisions are somewhat empirical, but were made after careful measurements and taxonomic considerations (magnification, enlargement and metaphase figures being kept constant), comparing parental karyotypes to the hybrids. Lines 4.12-Z and also 4.43-Z are known to contain functional human enzymes[8]. All lines were cultured in selective media of the following composition: MEM supplemented with 15% foetal calf serum (Flow), 10^{-3} M glutamine, 10^{-9} M hypoxanthine, 4×10^{-7} M methotrexate, 1.6×10^{-5} M thymidine, 100 IU/ml. penicillin and 100 μg/ml. streptomycin. Cells were harvested from plates and/or rollers at confluency.

that isolated from a variety of mouse cells. No "hybrid" or aberrant forms of circular DNA occurred.

The fact that apparently only mouse M-DNA is present in these hybrids may have several explanations. The two most plausible contributing factors are as follows. (1) The heterokaryon formed by the initial cell fusion did not contain viable human mitochondria or the contributions to the mitochondrial pool by each parental cell were grossly unequal. Since there is, at present, no way to check the relative species contribution to mitochondrial function in heterokaryons at the time of fusion, this hypothesis cannot readily be tested. (2) Human mitochondria or M-DNA in the human–mouse cell hybrids may be actively destroyed or, alternatively, diluted as a consequence of cell division, because they are not as effectively propagated as mouse mitochondria in the hybrid environment. A simple dilution phenomenon is adequate to explain the complete loss of human mitochondria from the human and mouse hybrids studied at the time of our analysis. In the case of the lines 4.12-Z, 4.43-Z, 3W4 and 4W10, the human donor cell was derived from peripheral blood white cells and was probably lymphocytic in origin. Such cells are known to be comparatively poor in cytoplasm and mitochondrial content and it is quite probable that the actual content of mitochondria in the initial hybrid had a strong mouse basis. On the other hand, there is no reason to expect a strong bias in HLE-C, which was derived from HeLa and 3T3 cells, or in the A9/Daudi hybrid, as HeLa and Daudi have a substantial number of mitochondria. We believe that the most likely explanation for our results is that a mixed population of mitochondria was present at the time of cell fusion, at least in some hybrids, but that the human mitochondria were either not propagated or more slowly propagated than the mouse mitochondria.

Attempts to solve this problem have been made by providing cultured cells with suspensions of pure mitochondria. In one experiment, mouse L cells were combined with intact human mitochondria. The mitochondria were rapidly incorporated in mouse cells, confirming similar experiments covering a wide range of species combinations[14]. Intracellular human M-DNA could be detected within several hours of combination and persisted for 72 h following, but was not detectable thereafter. A combination of mouse L-E cells (all circular dimers) with mouse L-929 mitochondria (90% monomer, 5% catenated dimer and 5% circular dimer) revealed 30% monomer M-DNA molecules at 24 h. At 72 h, only 5% monomers remained.

There are two possible reasons for the inability of human mitochondria, or human mitochondrial DNA, to subsist in the hybrid cell environment. First, components of mouse cytoplasm could in some way specifically or non-specifically interfere with the function or propagation of human mitochondria or their DNA. Second, the hybrid cell is, or rapidly becomes, deficient in human chromosomes carrying genes that are necessary for effective propagation of human mitochondria or their DNA. Even if only one human chromosome is needed for propagation of human mitochondria and their DNA, we may by chance have analysed no hybrid which contains the necessary chromosome. If two or more human chromosomes are required, then the chance that we have not analysed a hybrid with an appropriate chromosomal constitution is substantially increased. The identification of human chromosomes by their morphology without the use of quinacrine fluorescence or differential Giemsa staining is difficult and questionable, though the crude morphological classification does, in general, seem to correlate with the number of human enzymes expressed in the hybrids. Further work is clearly needed, with a greater variety of well characterized hybrids, to determine how many, and in what form, human mitochondria or mitochondrial components can be maintained in such hybrids. The possibility to isolate, and select for, mitochondrial mutants would be instrumental in such investigations.

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Relationship of Ochratoxin A to Foetal Death in Laboratory and Domestic Animals

BOVINE abortion is a major cause of economic loss to the dairy industry in the United States and elsewhere; estimates suggest that from 1.5 to 5.5% of all dairy cattle pregnancies terminate in abortions, the cause of which is largely unknown[1-3]. Many causes of bovine abortion are recognized[4] and diagnostic methods are well established, but in most laboratories only 20 to 30% of these abortions are diagnosed[1-7]. We report here the results of investigations of the possibility that feed contaminated with mycotoxin is a cause of previously undiagnosed bovine abortion. Recognized diagnostic procedures revealed the causes of twenty-six[8] out of fifty nonselected cases of bovine abortion referred to the Wisconsin State Animal Health Laboratory. Feed from the remaining farms was collected, dried, ground and fed to pregnant rats and rabbits to establish a possible relationship between feed and abortion. Feeds from several such herds induced foetal death and resorption in the test animals.

One such case merited more detailed investigation. During 2 months thirteen out of seventy-one cows had aborted, although previously no abortions had occurred in this herd for several years. No new animals had recently been introduced into the herd and conception and milk production had been outstandingly good. During the same period, sows and barn cats had also aborted The diet of these cows included farm-mixed ground feed concentrates and grains, corn silage, and visibly mouldy alfalfa-grass hay. When the hay was withheld from the diet, abortions ceased.

Major fungi isolated in pure culture from the mouldy hay were grown for 3 weeks on moist sterile corn seeds in 500 ml. Erlenmeyer flasks at room temperature, dried, finely ground in a Wiley mill and stored at 4° C before animal feeding trials or toxin purification. To detect toxic fungi, five, 35–50 g, unsexed Sprague–Dawley (Holtzman strain) rats per diet were housed in separate cages and fed individual cultures, or pooled mixtures of several cultures, *ad lib.* for 12 days. In most trials, 25% sucrose by weight was added to test diets to improve palatability. The five untreated control animals in each trial received only ground Rockland mouse/rat diet (Teklad, Inc., Winfield, Iowa). Toxic cultures from these trials were then individually fed *ad lib.* to five 10 day pregnant rats in a mixture of one part ground culture and three parts Rockland mouse/rat diet until day 20–21 of gestation when all animals were killed, their uteri removed and opened, and the number of living young or foetal resorption sites counted. Subsequent feeding trials with the foetal resorption-inducing fungus and its purified metabolites were performed in a similar fashion except that the total dose was administered by intubation on day 10 of gestation.

In the initial toxicity trials with pooled cultures no mortality occurred in control animals or animals fed cultures in group *A* (*Aspergillus terreus* Thom, *Aspergillus fumigatus* Fresenius, and *Penicillium oxalicum* Currie and Thom), or group *C* (*Aspergillus clavatus* Desmazieres, *Aspergillus flavus* Link and an unidentified, nonsporulating fungus). After 7 days, however, animals fed group *B* cultures (*Aspergillus niger* van Tieghem, *Penicillium cyclopium* Westling, *Stemphyllium botryosum* Wallr., and *Aspergillus ochraceus* Wilhelm began dying and all were dead by day 13 (1 day after tests were concluded). When fed individually, four of the cultures (*A. fumigatus*, *A. ochraceus*, *S. botryosum* and *P. oxalicum*) killed nearly all test animals in 12 days. Acute toxicity was apparently not directly related to foetal resorption activity since only one of the toxic cultures (*A. ochraceus*) caused a significant incidence of foetal death and resorption when fed at sublethal levels to pregnant rats from the tenth day of gestation (Table 1). Repeated trials with *A. ochraceus* corn cultures administered by intubation as a single dose on day 10 of gestation yielded similar results. Chloroform extraction of the ground *A. ochraceus* cultures followed by thin-layer chromatography (TLC) with a quantitative standard revealed large quantities of ochratoxin A (7-carboxy-5-chloro-3,4-dihydro-8-hydroxy-3-methyl-isocoumarin linked through the 7-carboxy-group to L-phenylalanine by an amide bond)[9].

Table 1 Foetal Death and Resorption in Rats receiving Sublethal Doses of Dried, Ground Corn Cultures of Toxic Fungi isolated from Mouldy Hay

Toxic fungi	Pregnant animals	Total implantations	Foetuses dead or resorbed No.	%
Penicillium oxalicum *	5	57	1	1.8
Stemphyllium botryosum †	2	6	1	16.7
Aspergillus fumigatus †	3	27	5	18.5
Aspergillus ochraceus *	5	43	43	100.0
Controls ‡	6	48	5	10.4

Animals were fed beginning on day 10 of gestation and killed on day 21.

* One part ground culture and three parts ground Rockland mouse/rat diet fed *ad libitum*.

† Cultures fed by intubation as a single 4 g dose because of unpalatability.

‡ Ground Rockland mouse/rat diet fed *ad libitum*.

Purified ochratoxin A was prepared as described by Van Walbeek *et al.*[10] to determine its effects on foetal death and resorption. Concentrations were quantified by ultraviolet absorption using the molar extinction at 333 nm in the acidic range in 95% ethanol $\left(\varepsilon_{333\ \mathrm{nm}}^{\mathrm{EtOH}} = 6{,}100\right)$[11]. Ten-day pregnant rats were force-fed ochratoxin A in 0.5 M sodium bicarbonate solutions at the rates of 0, 6.25, 12.50 and 25.0 mg/kg body weight. Other 10 day pregnant rats were treated with 18 mg/kg dihydroisocoumarin (5-chloro-3,4-dihydro-8-hydroxy-3-methyl-isocoumarin-7-carboxylic acid), a metabolic breakdown product of ochratoxin[12]. This dose approximates the amount of dihydroisocoumarin present in 25 mg/kg of ochratoxin A. Purified ochratoxin A at all doses induced foetal death and resorption (Table 2 and Fig. 1), but its hydrolysis product, dihydroisocoumarin, had no effect at the dose utilized.

Table 2 Influence of Different Doses of Ochratoxin A and Dihydroisocoumarin on Foetal Death in Rats when Administered by Intubation as a Single Dose on Day 10 of Gestation

Treatment	Dose (mg/kg)	Pregnant animals No.	Total implantations	Foetuses dead or resorbed No.	%
Ochratoxin A *	6.25	6	53	13	24.6
	12.50	7	88	72	81.8
	25.00 †	7	49	38	77.6
Dihydroisocoumarin *	18.00	4	45	0	0
Control ‡	0.00	7	35	3	8.1

* Ochratoxin A and dihydroisocoumarin administered in 0.5 M sodium bicarbonate solutions.

† Eleven living foetuses and one resorption site were present in a single dam. All other animals administered at this dose resorbed all of their foetuses. Another dam in this treatment group died within 48 h of treatment and embryos could not be counted because of massive utero-placental haemorrhage with dissolution of foetuses and placentas.

‡ Controls received 0.5 M sodium bicarbonate solutions.

Foetal resorption in rats has been related to various compounds and factors[13-16], although links with mycotoxin are limited. LeBreton *et al.*[14] reported the induction of utero-placental haemorrhage and foetal death in rats injected intra-

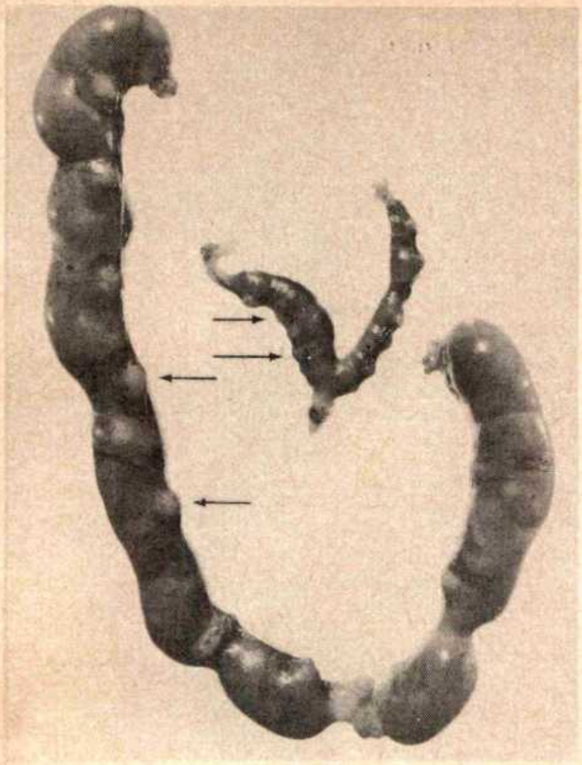

Fig. 1 Uteri removed from female rats on day 20 of gestation. The upper uterus from a rat receiving 12.5 mg/kg body weight ochratoxin A on day 10 of gestation contains eleven resorbing foetuses. The lower uterus from an untreated control contains 11 normal foetuses. Arrows indicate some of the implantation sites.

peritoneally with 300 μg of aflatoxin B_1, which has also been reported to induce foetal resorption, without apparent haemorrhage, in hamsters and mice[17]. Butler and Wigglesworth, however, failed to produce foetal resorption[18] when they administered 1 mg of aflatoxin B_1 orally to 180 g Wistar rats.

Aspergillus ochraceus and its major toxic metabolites have been investigated[9,19–21] intensively, but, in spite of the widespread occurrence of this fungus on feeds and foods, it has never been associated with animal or human health problems. Reports of ochratoxin A production by *Penicillium viridicatum*[10,22] may be of considerable practical significance, for this fungus is often isolated from mouldy corn and has been associated with renal damage in swine[23–24]. Ochratoxin A has been reported as a natural contaminant (0.11–0.15 p.p.m.) in poor grade corn in storage, but *A. ochraceus* could not be isolated from these samples[25]. The present investigations seem to be among the first to associate *A. ochraceus* and ochratoxin A with an important practical toxicological problem. These findings may be particularly important not only because of the economic loss to dairymen, but because other lactating animals in the aborting herds are consuming the same feeds and their milk is being sold for human consumption. It is not known whether cattle can excrete ochratoxin A or its metabolites in milk as is the case with aflatoxins[26–30].

The relationship between ochratoxin A-induced foetal death in rats and mouldy-hay-related abortion of cattle remains to be clarified. The large quantity of ochratoxin A necessary to duplicate dose-response effects in pregnant rats has not been available for dairy cattle studies. Preparation of ochratoxin A for this purpose is in progress.

We thank Professor Kenneth Raper for confirmation of the identity of *Penicillium* and *Aspergillus* species, and Dr Fun Sun Chu for analytical reference standards of ochratoxin A and dihydroisocoumarin. This research was supported by the College of Agricultural and Life Sciences, University of Wisconsin, and by a US Public Health Service research grant and a US Department of Agriculture Hatch Act Project.

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Stress, Fighting and Neuroendocrine Function

EVIDENCE of a relationship between pituitary hormones and aggressive behaviour is provided by the observation[1] that increased concentrations of the luteinizing hormone (LH), produced either by exogenous administration or by castration, promote aggressive behaviour and dominance in male starlings. Concentrations of pituitary adrenocorticotrophic hormone (ACTH), plasma corticosterone[2] and of plasma LH[3] are also increased in defeated mice.

We have examined plasma concentrations of ACTH and adrenocortical steroids in rats after testing in the shock-induced fighting paradigm[4]. Control animals were shocked individually to assess the pituitary-adrenal effects of electric shock alone.

Long-Evans male rats ($n=216$, Simonsen, Gilroy, California) approximately 80 days old and housed individually with free access to food and water were used. Experiments were done between 0800 h and 1000 h during the lights-on part (0700 h–1900 h) of a 12 h cycle of light and dark.

Testing chambers (17.8 × 17.8 × 30.5 cm), programming equipment and procedure were as described previously[5]. Each of eight experiments involved at least three groups. Those in the fight (F) group were placed in the chamber in pairs and administered ninety electric shocks through the footpads in each 4.5 min session. Animals in the shock (S) group were treated identically except they were placed individually in the chamber. There was also at least one non-shocked control group.

Animals were decapitated and blood was collected from the trunk into chilled heparinized tubes for plasma ACTH and corticosterone determinations. Within 1 h, the blood was centrifuged (2,500 r.p.m. for 15 min) and the plasma frozen. A fluorometric micro-method[6] was used for plasma corticosterone determinations. Plasma from at least five animals was pooled by treatment groups, and bioassayed for ACTH[7].

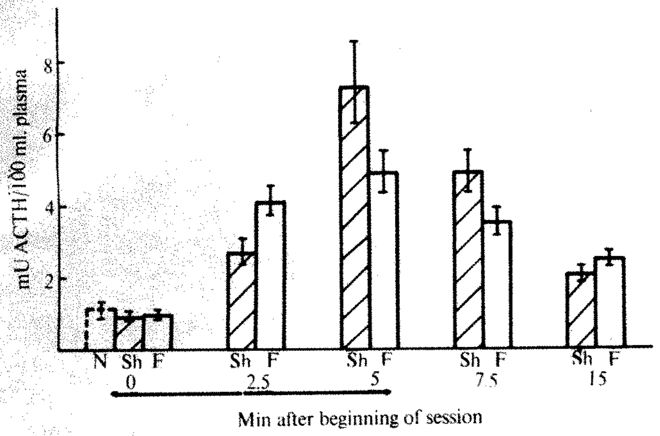

Fig. 1 ACTH time course day 3 (experiment 5) for non-shock control animals (N), individually shocked animals (Sh), and for fighting animals (F).

In experiments 1–5, three sessions were administered at 48-h intervals. In experiments 1–4 the animals were killed after the 4.5 min session on day 3. Control animals were handled and weighed daily. To monitor pituitary-adrenal acitvity further, animals were killed at four time points in experiment 5. For one subgroup the session was interrupted and the rats killed after fifty shock trials (2.5 min time point). Animals in the second subgroup were killed after the conclusion of the ninety trial session (5 min point). Animals in the third and fourth subgroups were returned to the animal room after the session and killed 2.5 or 10 min later (7.5 and 15 min points, respectively).

Table 1 Plasma ACTH Values (mU/100 ml.) and 95% Confidence Limits from End of Session (5 min)

Experiment	Day	Group N	 S	 F
1	3	0.51 (0.19—1.00)	9.36 (4.52—32.06)	3.11 (1.84—5.43)
2	3	0.90 (0.79—1.02)	8.96 (7.74—10.69)	9.33 (8.03—11.18)
3	3	1.40 (0.73—2.09)	4.89 (3.19—9.03)	2.76 (1.92—4.22)
4	3	1.38 (0.72—2.01)	11.68 (6.48—34.38)	5.60 (3.76—10.52)
5	3	1.02 (0.90—1.15)	7.21 (6.24—8.53)	4.89 (4.39—5.52)
6	1	1.27 (0.64—1.88)	4.27 (2.91—7.20)	3.71 (2.52—5.97)
7	1	0.89 (0.78—1.00)	9.26 (7.95—11.11)	6.20 (5.50—7.12)
8	1	0.65 (0.42—0.91)	7.69 (5.50—13.04)	2.07 (1.53—2.85)

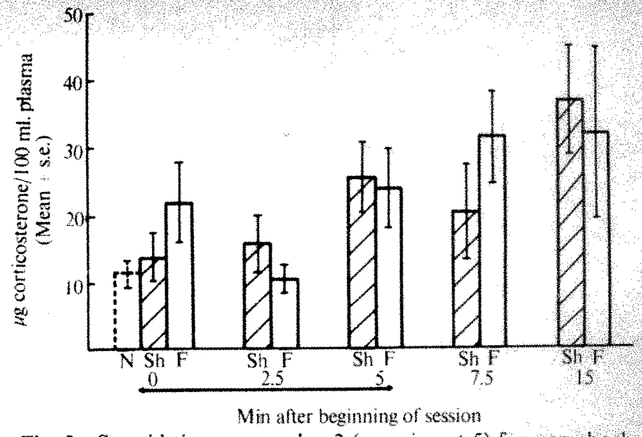

Fig. 2 Steroid time course day 3 (experiment 5) for non-shock control animals (N), individually shocked animals (Sh), and for fighting animals (F).

In experiments 6, 7 and 8, there was only one testing session. Experiment 6 was otherwise identical to experiments 1–4, and experiment 7 was otherwise identical to experiment 5. In experiment 8, one control group was the same as that used in the previous experiments, that is, the animals were simply handled and weighed daily (N). Animals in the second and third control groups were placed in the chamber for 4.5 min either singly (group C) or in pairs (group C2) but not shocked. The animals in the fourth control group were individually placed in chambers and the shock was delivered to both chambers from a single shocker (group S2).

Paired animals fought on approximately 40% of the shock trials. In every case, plasma ACTH at the end of the session for both S and F groups was significantly above controls (group N). Further, in six of the eight experiments, animals in the S group exhibited significantly higher concentrations of plasma ACTH than animals in group F (Table 1).

On day 3 ACTH levels for group S were higher than the F animals 7.5 min but not 15 min after the beginning of the session (Fig. 1). At 2.5 min, however, the difference between groups S and F was in the opposite direction. On day 1, F animals were lower or not different from S animals at every time point (Fig. 3). There were no significant differences between groups in plasma corticosterone levels (Figs. 2 and 4).

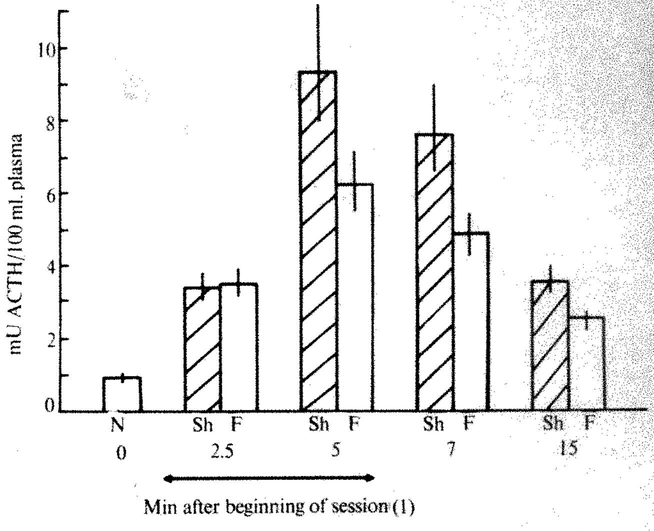

Fig. 3 ACTH time course day 1 (experiment 7) for non-shock control animals (N), individually shocked animals (Sh), and for fighting animals (F).

The higher ACTH levels of the S animals cannot be accounted for on the basis of differences in the physical aspects of the electric shock. Whether one or two rats were shocked individually from a single shock source, the S animals were still significantly higher than the F animals, and the former groups were not different from each other (Fig. 5). Nor did the simple pairing of animals for 4.5 min without shock evoke a significant ACTH response.

Fighting behaviour in mice[2] and electric shock in rats and mice[8,9] have been shown to evoke increased pituitary-adrenal activity. The combination of shock and fighting might be expected to elicit a greater pituitary-adrenal response than either stimulus alone. The finding that fought rats have lower plasma ACTH than shocked animals is therefore particularly interesting. Plasma corticosterone concentrations were more variable and only suggested possible differences in hypothalamo-hypophyseal activity. It seems that direct measures of ACTH and other pituitary hormones might provide more reliable data in studies designed to elucidate neuroendocrine-behaviour relationships.

It seems unlikely that differences in plasma ACTH between the shocked and fought groups reflect a difference in skeletal-motor responses evoked by electric shock. During initial presentations of shock, animals in each group were virtually indistinguishable in this respect. Shortly after initiating the shock train, however, paired animals would typically assume a stereotyped posture raised up on their hind legs facing one another. Vigorous skeletal-motor and vocal responses to shock were still evident but, rather than engaging in what seemed to be disorganized escape attempts, the animals would direct attacks toward each other. Thus, the groups differed in the pattern of activity rather than overall level of activity. Present results therefore suggest that the magnitude of the neuroendocrine response following exposure to aversive stimulation is a function of the behaviour engaged in by the animals rather than simply the intensity of the aversive stimulation.

Using the same shock-induced fighting paradigm, Stolk *et al.*[10] have found that immediately after the session, shocked rats showed significantly increased norepinephrine turnover in the brain stem, while fought animals were not significantly different from controls. Weiss *et al.*[11] found that whole brain catecholamine concentrations were higher in animals that could escape and/or avoid electric shock than those that could not. They suggested that psychological aspects of the stressful situation are important in determining the effects of shock on physiological function[12]. Our studies provide neuroendocrine data which are consistent with this view.

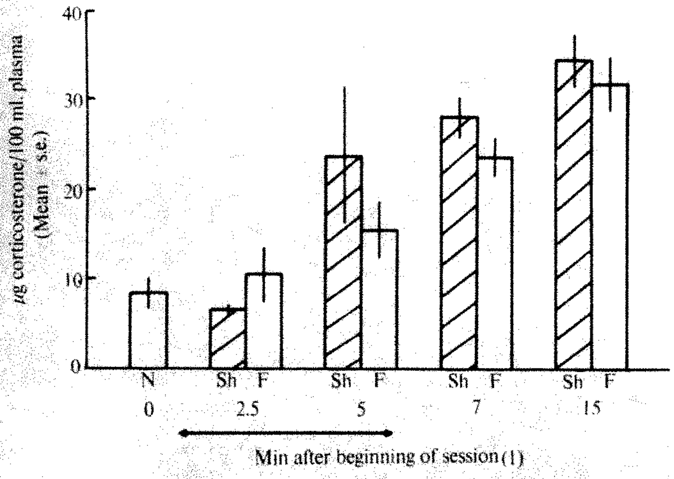

Fig. 4 Steroid time course day 1 (experiment 7) for non-shock control animals (N), individually shocked animals (Sh), and for fighting animals. (F).

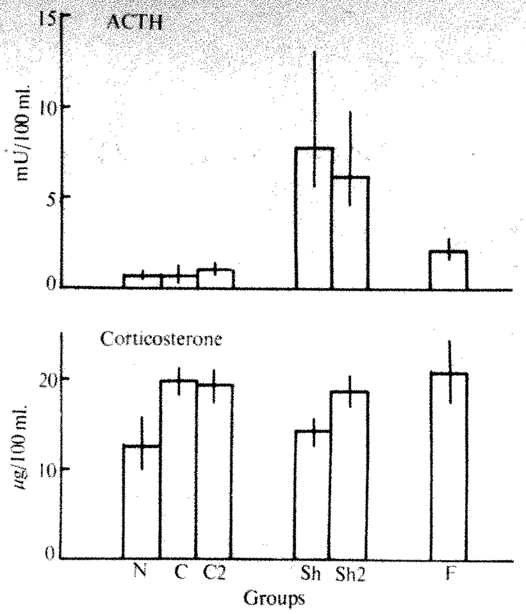

Fig. 5 ACTH and steroids for all groups in experiment 8. The bars represent 95% confidence intervals and s.e. of the mean, respectively. The non-shocked animals were killed after removal from the living cages (N), or after being placed in the chamber for 5 min individually (C) or in pairs (C2). The individually shocked animals were administered shock from a single shock source (Sh) or from two shockers (Sh2).

These data indicate that the pituitary-adrenal response can be attenuated by the expression of an organized pattern of behaviour. Thus it seems that if a behavioural release mechanism exists, the expression of these behaviours can reduce the magnitude of the internal response, both in the pituitary-adrenal system and brain amines. This mechanism can serve an adaptive function by dampening the internal response which may be excessive and have damaging consequences.

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BOOK REVIEWS

Sanity on Science

Scientific Knowledge and its Social Problems. By J. R. Ravetz. Pp. x+449. (Clarendon: Oxford, September 1971.) £5.00.

THIS book is too good for its argument to be summarized for those too lazy to read it for themselves. It is too rich and profound in detail to survive such discourtesy, and contains no obscurities to be reinterpreted. All that need be said in general is that it is thoughtful, incisive, scholarly, lucid, humane and sane. Everyone—but everyone—within or concerned about science should read it slowly and carefully.

Having said this, I am not going to niggle, or damn here and there with faint praise. I agree so completely with the spirit and style of the book that I prefer simply to express admiration for the best sections by "starring" the relevant pages. A more fruitful approach than criticism is to suggest how we might further extend and strengthen Dr Ravetz's conclusions in various ways.

Along the "philosophical" or "intellectual" axis, for example, the abstractness and artificiality of the "problems" that scientists solve (*109–140) could be linked very beautifully to Stefan Körner's demonstration of the essential distinction in logical structure between experience and theory. The concept of a "fact" (*181–208) could also be carried further by noting that inter-subjective pattern recognition, as in the biological sciences, is just as good a basis for consensibility as formal mathematical logic. The whole question of criteria for scientific arguments then has a much broader answer, and we can escape from the narrow intellectual method of physics as the paradigm of science. Thus, the notion of a "tool" (*88–94) applies not merely to particular results or techniques carried across interdisciplinary boundaries but to a whole intellectual viewpoint. Instead of talking of biophysics, we should be referring to "physicobiology". Such interconnexions could never provide a bedrock for the tacit and obscure foundations (*209–222) of the natural sciences, but they would, I believe, help to discriminate against "folk sciences" (*386–402), bogus expertise (*349–356) and other unreliable claimants to precise knowledge (*364–386).

On the other hand, the sheer difficulty of getting any reliable results at all, even in the most mature sciences, cannot be overstated. The craft of research (*94–108) has its delights, but it is also immensely demanding. It would be instructive to analyse the older literature to find out whether there really was a smaller proportion of rubbish being published than we complain about nowadays. We might also try to distinguish between the mass-produced products of industrialized science and the equally shoddy work of incompetent half-trained cottage craftsmen in countries without a long scientific tradition.

Again, the hypothesis of the élitist, class basis of the morale of the individual scientist (*58–68, *159–168) might stimulate many further factual (and fanciful) investigations. It is possible, for example, that team research—the most obvious manifestation of industrialization—takes the moral pressures and strategic responsibilities off the back of the team member, and loads it on to the group as a whole, or on to its leader. In this context, the distinction between craftsman, technician and scientist (*140–145) becomes blurred—and yet more significant than ever.

We must also look at the whole range of mechanisms by which quality is controlled within the scientific community (*272–280). Job patronage is often just as effective as the referee system; the personal internalization of the tension between "internal" and "external" values (*165–166) in the apprenticeship phase was the secret of the high academic standards of the old German professoriat. That is why rapid expansion can lead to corruption (*411–420), especially if the rewards of scholarly success are set too high. Shouldn't we be referring in some cases to the "commercialization" of science, rather than its "industrialization"? Just as there can be a national style of research, so there can be a national version of scientific etiquette (*289–313) accommodated to the moral standards of the social system in which it is embedded. To see science at its most pathological, one should look at it inside a totalitarian state; but even there, although completely bureaucratized and "politicized", it retains a peculiar self-healing power (*410–411) comparable only with the power of spiritual regeneration to be drawn from the gospels of Jesus of Nazareth.

How near can we come, eventually, to some sort of stable relationship between the scientific group and humanity in the large? The unsettling factor is not necessarily technology—which has its own deep roots, needs and style—nor romantic irrationality. We must reckon with the infinite human capacity for rationalization, by which any selfish interest can be justified, any crime legalized, and any folly explained. As I said—good, reliable, scientific results are hard to get; and yet we are all anxious to live and act for the best, according to some system. This could be the secret of our willingness to entrust our practical problems (*339–363) to half-baked experts, instead of adopting the sceptical, uncommitted, hard-headed attitude appropriate to a scientific approach. Whether or not "critical science" (*422–436) itself can stiffen us up, and help society protect itself from its own abuses, must still be reckoned an open question. At least we may, through books like this, achieve a new level of self-critical science. As Dr Ravetz remarks, "To thread one's way through these pitfalls, making a genuine contribution both to scientific knowledge and to the welfare of society, requires a combination of knowledge and understanding in so many different areas of experience, that its only correct title is wisdom". If he will allow me to say so—I think he has guided us for a few steps safely through the labyrinth.

JOHN ZIMAN

Chemistry in Industry

High Polymers. By Peter Tooley. (Chemistry in Industry.) Pp. 215. (John Murray: London, September 1971.) £2.50 cloth; £1.50 paper.

Fats, Oils and Waxes. By Peter Tooley. (Chemistry in Industry.) Pp. 182. (John Murray: London, September 1971.) £2.25 cloth; £1.25 paper.

Fuels, Explosives and Dyestuffs. By Peter Tooley. (Chemistry in Industry.) Pp. 248. (John Murray: London, September 1971.) £2.75 cloth; £1.75 paper.

Food and Drugs. By Peter Tooley. (Chemistry in Industry.) Pp. 280. (John Murray: London, 1971.) £2.85 cloth; £1.85 paper.

THESE fascinating volumes total a few pages more than the 1967 edition of Shreve's *Chemical Process Industries* which, because of its different format, carries some two to three times as much material per page. Since its first edition in 1945 "Shreve" has been the classic single volume reference and student text in this field, and many more than 100,000 copies have been sold. This book outlines the background and traditions of the chemical engineer.

But if Shreve presents in his treatise and textbook for students the sinew and bone of the culture of the industrial chemist and the chemical engineer, Tooley presents, in a much less rigorous and formal way, the heart and soul of this same culture. He states that his aims are (*a*) to write primarily as a source book for science teachers, (*b*) to provide teachers with relevant background material, (*c*) to keep them abreast of events, and (*d*) to build a bridge between school and industry.

Tooley, in excellent prose, tells teachers how to butter in between the blocks of scientific facts a smoothing mortar of human interest. Thus he tells hundreds of stimulating stories of historical research and development accomplishments leading to important processes and products. These may or may not involve chemistry in industry. As an example, under "Pain Killers" he recounts that the first surgical operation was only after Adam had been caused to fall into a deep sleep. Then the Lord God removed one of his ribs and closed up the flesh. Next the success of mesmerism as a pain killer is discussed; and the historical, physiological and psychological aspects in the use of pain killers and related drugs are presented with more attention than is given to their chemistry. The broadened picture is well detailed to give another intriguing story.

The volumes are eminently readable with a delightful presentation of facts in most interesting style, here and there illuminated with cuts made one hundred or two hundred years ago as well as numerous photographs and line drawings. As in any book of whatever size which comprehends such a wide scope of the horizons of human knowledge, one finds what one finds—without any surety of prediction. In searching, the reader will, as apt as not, find many other charming stories to fill out his store of knowledge. Thus there are 40 pages on fat technology, 50 pages on detergents and polishes, also 66 pages on cosmetics, more on chemical materials than on their chemistry.

The numerous figures, printing, and binding are well done. The small, almost pocket, size of 5½ in. × 9 in. is convenient.

The books would not be recommended for the textbook of any course, nor as the only source of information for any examination. But they certainly will be excellent and very easily read supplementary material for science or engineering students at any level or for professionals and others who are concerned for any reason with chemistry in industry.

Donald F. Othmer

For the Fish Watcher

Fishes of the Sea. By John Lythgoe and Gillian Lythgoe. Pp. 320 (212 photographs). (Blandford: London, October 1971.) £3.

Fishes of the Sea is basically a book for the underwater swimmer and fish watcher. The authors are underwater swimmers of experience and are thus well acquainted with the problems of identifying a fish seen at a distance or at an awkward angle. The coloured photographs are of excellent quality and cover most of the orders included in the book.

From this aspect *Fishes of the Sea* will no doubt be deservedly appreciated, for underwater pictures of fish can be as aesthetically satisfying as they are useful for identification. There seems, however, to be a tendency on the part of publishers to select photographs taken underwater (as opposed to photographs of fish in aquaria) at all costs. This book is no exception, for here we have half-visible fish concealed by benthic growths, as in Fig. 75, of *Crenilabrus cinereus*; fish half seen in the distance (Fig. 88 of *Auxis thazard*), and a whole page picture of a clearly seen swimmer and a shoal of quite indistinguishable fish. If the purpose of the photographs is to help the underwater observer to identify the fish he sees, these pictures fail. There is, moreover, the curious aspect that while pains are taken to suggest that most of the photographs are taken by underwater photographers, a considerable number are quite obviously of captive fish in aquaria. Two are in fact of dead fish out of water! One of the aquarium pictures, of *Remora remora*, is even wrongly identified, for the shark sucker pictured is clearly *Echeneis naucrates*.

The book includes all the common fish (and a number of rather uncommon ones too) found in the coastal waters of Europe, including the Baltic and the Mediterranean. For each species notes are given on distribution and biology, with a formal description of morphology and coloration. Many groups are illustrated by simple outline drawings of the common species with notes on identification side by side on the same page, a useful and thoughtful arrangement to help in identification. The drawings throughout the book are simple outlines with an absolute minimum of detail except for distinctive features of form or colour pattern. In places one feels the simplification has gone too far, as for example in the omission of the lateral line in drawings of about half the wrasses (*Labridae*), and the absence of pelvic fins in *Thunnus thynnus*, *Auxis thazard* (the related species are shown as possessing them), and *Chirolophis ascanii*, all species with well developed pelvic fins. These omissions can only confuse the inexperienced user of the book.

It is disturbing to find the publishers advancing this book on the dust jacket as "scientifically authoritative", for its text contains a high proportion of errors of one kind or another. For one thing users of a book so described might expect to be spared such unorthodoxies as cartilagenous (thrice), oviperous, ovoviviperous, and viviperous (once each) on a single page (22). Distributional data are often incorrect, for example in the failure to indicate that *Callionymus reticulatus* is a North Sea species (where it is fairly common); and to say that Ray's bream (*Brama brama*) is not common north of Biscay, though solitary specimens are usually encountered in winter is not a true picture of its occurrence in northern waters. Other errors, such as the statement that there is only one species in the family Coryphaenidae and that *Alopias* has both nictitating membrane and a spiracle, together with frequent misspellings of scientific names of fishes, destroy any claim of this book to be authoritative.

Alwyne Wheeler

Josephson Introduced

An Introduction to the Josephson Effect. By B. W. Petley. Pp. 88. (Mills and Boon: London, October 1971.) £2.50.

This little book is a careful, authoritative, but simple introduction to this rapidly expanding subject. It is heartening to see a first engineering text in this field of so much engineering promise, and to see it clearly written, free of mistakes, and surprisingly complete on the basic science side.

Having said as much, may I complain that at £2.50 the book is somewhat too little, coming almost precisely to 3p per very small page. At this price I would have liked to see more material, and more of it specifically pointed towards engineers. For example, a discussion of mechanical analogues, which I have found very useful in talking to engineers (and physicists) as well as in thinking about devices, would be in order. Some discussion of McCumber's damping theory (although the use of damping in devices may be too recent to have got in) would be useful. Most of all, it seems to me that the four pages devoted to "Other Applications", such as Matisoo's ideas on switching, are entirely inadequate in a book for engineers.

Let me not close with a negative impression. This will be a very handy book to have on one's shelves as we enter the era of extensive practical applications of the Josephson effect.

P. W. Anderson

CORRESPONDENCE

Academic Freedom

SIR,—The Tenth Conference on Slavic Studies with the theme "Croatian Nation and Croatian Exodus—investigation of effects after 100 years of emigration" was held at Case Western Reserve University, Cleveland, Ohio, November 26–28, 1971. The participants and sponsors issued at the conclusion of the conference the following statement:

We deeply regret the last minute changes in circumstances and decisions that prevented the attendance of the scheduled conference speakers from Yugoslavia: Professor Dr Ljudevit Jonke, Croatian University, Zagreb, and President, Matica Hrvatska; Professor Dr Ivo Baucic, Croatian University, Zagreb; Professor Andjelko Runjic, Croatian University, Zagreb, and Professor Ivan Cizmic, Historical Institute, Matica Iseljnika Hrvatske, Zagreb.

Such occurrences are contrary to generally accepted practice of cultural exchanges intended to further understanding, cooperation and peace in the world.

We believe that academic freedom and international exchange of scholarship should not be infringed upon under any circumstances.

We are, however, confident that exchanges between American scholars in general, and those of Croatian descent in particular, and their colleagues in Croatia will be frequent and fruitful in the future.

TEFKO SARACEVIC
President, American Croatian Academic Club,
General Chairman of the Conference
VLADIMIR RUS
Chairman, Department of Slavic and East European Languages,
Case Western Reserve University
MICHAEL S. PAP
Director, Institute for Soviet and East European Studies,
John Carroll University
DUSKO I. DUISIN
President,
Croatian Academy of America
VICTOR KOLUDROVICH
President,
Croatian Foundation of America

Obituary

Professor G. W. Harris

THE death of Geoffrey W. Harris, Dr Lee's Professor of Anatomy in the University of Oxford, on November 29, 1971, deprives British endocrinology of a scientist of world stature who did much to clarify the relationships between the brain and endocrine system and so lay the foundations of the subdiscipline of neuroendocrinology. The work which made his name was the discovery of the functional significance of the hypophyseal portal vessels linking the brain and pituitary gland. He was also deeply involved in the isolation of the chemical agents that control the output of anterior pituitary hormones, the releasing factors.

While a student at Cambridge in 1935 Harris became greatly interested in the work of F. H. A. Marshall, who had drawn attention to the observations establishing that environmental stimuli influence reproductive function in numerous species, and was led to investigate the physiological basis of these effects. Marshall had shown with E. B. Verney that diffuse electrical stimulation of the brain of anaesthetized female rabbits frequently caused ovulation and suggested to Harris that the effects of localized electrical stimulation of the hypothalamus merited study. In due course the demonstration that excitation of the hypothalamus elicited gonadotrophin secretion launched Harris on his life's work.

Since it was then believed that many neuroendocrine responses were slow to become manifest, and that prolonged stimulation of the brain was required to elicit them, Harris devoted much time and ingenuity to developing a method for the inductive stimulation of the brain in freely moving and conscious animals. This was long before the development of radio-controlled devices. Because the generation of massive electromagnetic fields was necessary, the equipment was spectacular in operation, although the rabbits housed in it remained undisturbed. At first, attention was directed toward the activities of the neurohypophysis, the control of milk ejection and uterine motility, but later the control of adrenal and thyroid gland function came under scrutiny.

In parallel with this work the nature of the functional link between the brain and pituitary gland was being determined. Although it was expected that nerve fibres would transmit stimuli from the nervous system to this endocrine organ, the necessary nerve fibres in the anterior pituitary proved extremely difficult to demonstrate convincingly and the possibility that the hypophyseal portal vessels could provide an alternative pathway remained speculative, although J. D. Green and Harris had been able to demonstrate that blood flowed from the median eminence to the pituitary gland.

Previous workers had examined the effect of section of the pituitary stalk on the secretion of pituitary hormones with contradictory findings, but Harris in 1950 established that rapid regeneration of the portal vessels occurred after transection and that the level of pituitary function could be related to the degree of vascular reconnexion. Prevention of regeneration of the system by the insertion of a waxed paper plate was associated with a consistent depression of pituitary function.

The special character of the blood derived from the median eminence of the hypothalamus was next established in work with Dora Jacobsohn by removing the pituitary gland of rats and then placing pituitary tissue either in contact with the median eminence or under the temporal lobe of the brain. Only those animals with grafts made to the median eminence showed a return of pituitary function, although in both locations the transplant was nourished by blood vessels derived from the brain. This work also indicated that the cyclic pattern of gonadotrophin secretion seen in the female, as opposed to the constant release in the male, is due to differences in hypothalamic activity.

As soon as it appeared that neurohumoral agents from the hypothalamus were discharged into the portal vessels for transmission to the anterior lobe of the pituitary to affect the secretion of hormones, experiments aimed at the isolation of these factors began. Harris and his collaborators in 1960 obtained an acidic extract of median eminence tissue that evoked ovulation in the rabbit, but progress in this field proved slow and the identification of this factor eluded them. Quite recently the structure of porcine luteinizing hormone releasing factor was announced by A. V. Schally and his colleagues in New Orleans, an important step towards obtaining a synthetic molecule.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Proceedings of the Royal Irish Academy. Vol. 71, Section B, No. 11: The Petrology, Chemistry and Structure of the Galway Granite in the Rosmuc Area, Co. Galway. By C. W. Claxton. Pp. 155–170. 34p. Vol. 71, Section B, No. 12: The Post-Dalradian Strata Along the North-West Coast of Lough Foyle, Inishowen, Co. Donegal. By T. Murphy, D. G. G. Young and P. M. Brück. Pp. 171–182 + plate 7. 20p. Vol. 71, Section B, No. 13: The Present Distribution of the Bank Vole *Clethrionomys glareolus*. Schreber in Ireland. By J. S. Fairley. Pp. 183–190. 12p. (Dublin: Royal Irish Academy, 1971.) (2510

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Natural Environment Research Council. National Institute of Oceanography, Collected Reprints, Vol. 18. Reprints 725–777. (Godalming, Surrey: National Institute of Oceanography, 1971.) [2610

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Bulletin of the British Museum (Natural History). Entomology. Vol. 26, No. 4: Revisional Notes of African *Charaxes* (Lepidoptera: Nymphalidae), Part VII. By V. G. L. van Someren. Pp. 181–226 + 11 plates. £3.80. Vol. 26, No. 5: A Revision of the African Genus *Phylloxiphia* Rothschild and Jordan (Lepidoptera: Sphingidae). By A. H. Hayes. Pp. 227–243 + 11 plates. £1.60. (London: British Museum (Natural History), 1971.) [811

Building Research Station Digest, No. 135: Motorway Noise and Dwellings. Pp. 6. (London: HMSO, 1971.) 5p. [811

Royal Observatory Bulletins. No. 160: Results Obtained with a Danjon Astrolabe at Herstmonceux. II. Analysis and Discussion: Herstmonceux Astrolabe Catalogue. By D. V. Thomas and R. E. Wallis. Pp. 113–172. 85p net. No. 161: Rhw Proper Motions of RR Lyrae Variables, II. By S. V. M. Clube, Z. Aslan, T. W. Russo and E. D. Clements. Pp. 173–212. 55p net. No. 165: Motion of Ao Stars Perpendicular to the Galactic Plane. IV. Racial Velocities in the South Galactic Cap. By G. A. Harding, F. Fahim and C. Margaret Haslam. Pp. 259–271. 25p net. (Herstmonceux: Royal Greenwich Observatory, 1971.) [811

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